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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 7	AUG 27	USPATOLD now available on STN
NEWS 8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 10	SEP 13	FORIS renamed to SOFIS
NEWS 11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 16	OCT 19	BEILSTEIN updated with new compounds
NEWS 17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 18	NOV 19	WPIX enhanced with XML display format
NEWS 19	NOV 30	ICSD reloaded with enhancements
NEWS 20	DEC 04	LINPADOCDB now available on STN
NEWS 21	DEC 14	BEILSTEIN pricing structure to change
NEWS 22	DEC 17	USPATOLD added to additional database clusters
NEWS 23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 24	DEC 17	DGENE now includes more than 10 million sequences
NEWS 25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 29	JAN 02	STN pricing information for 2008 now available
NEWS 30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 31	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new

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                  custom IPC display formats
 NEWS 32  JAN 28  MARPAT searching enhanced
 NEWS 33  JAN 28  USGENE now provides USPTO sequence data within 3 days
                  of publication
 NEWS 34  JAN 28  TOXCENTER enhanced with reloaded MEDLINE segment
 NEWS 35  JAN 28  MEDLINE and LMEDLINE reloaded with enhancements

 NEWS EXPRESS  19 SEPTEMBER 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that
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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:49:32 ON 05 FEB 2008

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       1.26       1.26

FILE 'REGISTRY' ENTERED AT 15:52:55 ON 05 FEB 2008
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STRUCTURE FILE UPDATES:    4 FEB 2008  HIGHEST RN 1001463-85-9
DICTIONARY FILE UPDATES:   4 FEB 2008  HIGHEST RN 1001463-85-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

  Please note that search-term pricing does apply when
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REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
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on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html
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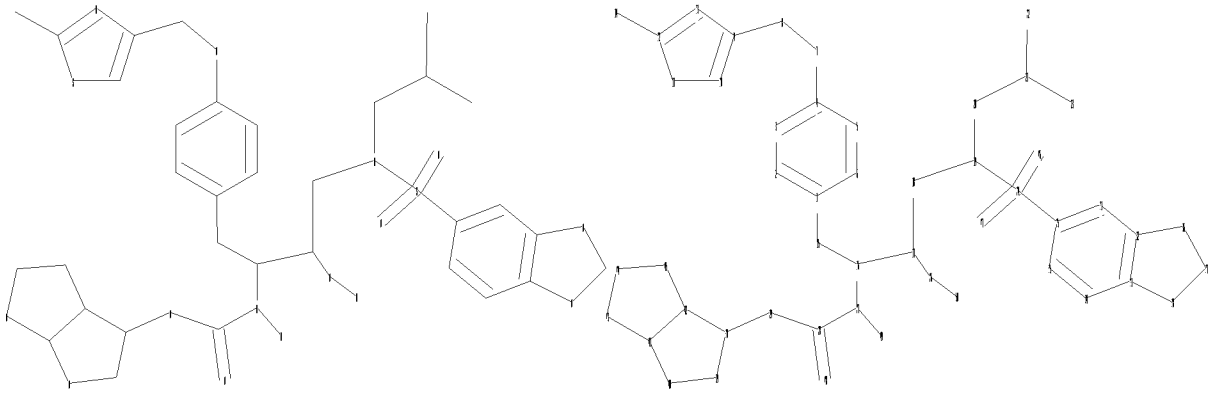

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7 8 14 15 16 17 18 19 20 21 22 23 24 26 27 28 29 46 47 48 49
50
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41 42 43 44 45
chain bonds :
1-15 4-7 7-8 8-9 12-14 15-16 16-17 16-27 17-18 17-26 18-19 19-20 19-24
20-21 21-22 21-23 24-25 24-46 24-47 26-50 27-28 27-49 28-29 28-48 29-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 9-10 9-13 10-11 11-12 12-13 25-31 25-35 30-39
30-42 31-32 32-33 32-36 33-34 33-38 34-35 36-37 37-38 39-40 40-41 41-42
41-43 42-45 43-44 44-45
exact/norm bonds :
4-7 7-8 9-10 9-13 10-11 11-12 12-13 16-27 17-26 18-19 19-20 19-24 24-25
24-46 24-47 27-28 28-29 28-48 29-30 30-39 30-42 32-36 33-38 36-37 37-38
39-40 40-41 41-42 41-43 42-45 43-44 44-45
exact bonds :
1-15 8-9 12-14 15-16 16-17 17-18 20-21 21-22 21-23 26-50 27-49
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 25-31 25-35 31-32 32-33 33-34 34-35

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:Atom 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom 35:Atom
36:Atom 37:Atom 38:Atom 39:Atom 40:Atom 41:Atom 42:Atom 43:Atom 44:Atom
45:Atom 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS

10560500.trn

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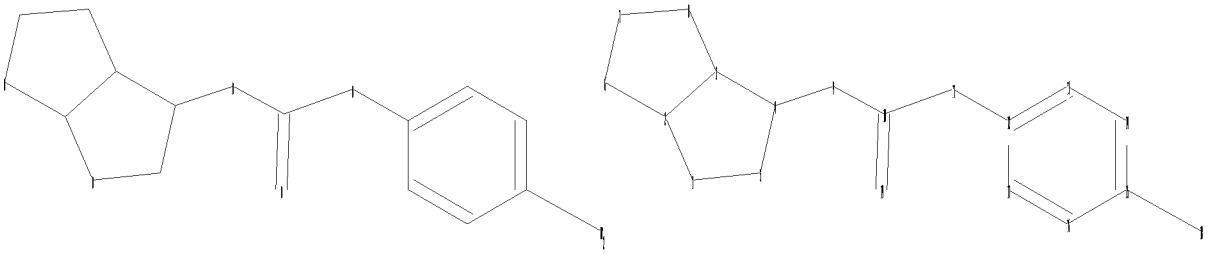

chain nodes :
9 10 11 18 19
ring nodes :
1 2 3 4 5 6 7 8 12 13 14 15 16 17
chain bonds :
4-9 9-10 10-11 10-19 11-12 15-18
ring bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 6-7 7-8 12-13 12-17 13-14 14-15 15-16
16-17
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 4-9 6-7 7-8 9-10 10-11 10-19 11-12
exact bonds :
15-18
normalized bonds :
12-13 12-17 13-14 14-15 15-16 16-17

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS

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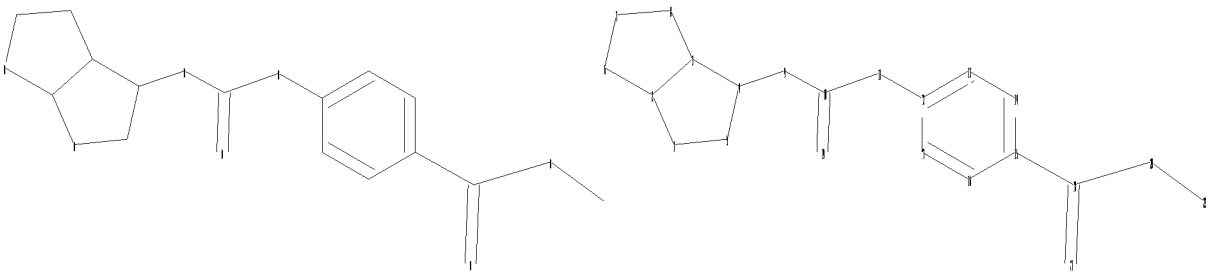

chain nodes :
9 10 11 18 19 20 21 22
ring nodes :
1 2 3 4 5 6 7 8 12 13 14 15 16 17
chain bonds :
4-9 9-10 10-11 10-19 11-12 15-18 18-20 18-21 20-22
ring bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 6-7 7-8 12-13 12-17 13-14 14-15 15-16
16-17
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 4-9 6-7 7-8 9-10 10-11 10-19 11-12 18-20
18-21 20-22
exact bonds :
15-18
normalized bonds :
12-13 12-17 13-14 14-15 15-16 16-17

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS

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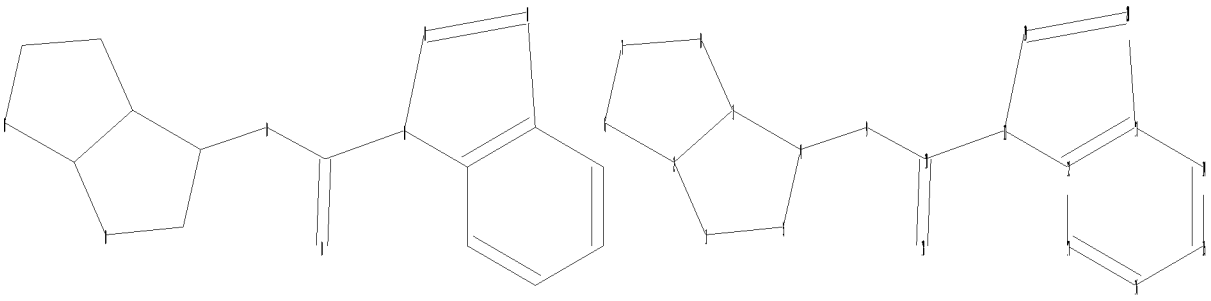

chain nodes :
9 10 18
ring nodes :
1 2 3 4 5 6 7 8 11 12 13 14 15 16 17 19 20
chain bonds :
4-9 9-10 10-11 10-18
ring bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 6-7 7-8 11-12 11-19 12-13 12-17 13-14
13-20 14-15 15-16 16-17 19-20
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 4-9 6-7 7-8 9-10 10-11 10-18 11-12 11-19
13-20 19-20
normalized bonds :
12-13 12-17 13-14 14-15 15-16 16-17

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom
20:Atom

L4 STRUCTURE UPLOADED

=> l1 exa
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SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 0 TO 0
PROJECTED ANSWERS: 0 TO 0

L5 0 SEA EXA SAM L1

=> l1 exa full
FULL SEARCH INITIATED 15:53:56 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 20 TO ITERATE

100.0% PROCESSED 20 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L6 2 SEA EXA FUL L1

=> l2 exa full
FULL SEARCH INITIATED 15:54:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

L7 8 SEA EXA FUL L2

=> l3 exa full
FULL SEARCH INITIATED 15:54:08 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2 TO ITERATE

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SEARCH TIME: 00.00.01

L8 1 SEA EXA FUL L3

=> l4 exa ful
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FULL SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

L9 1 SEA EXA FUL L4

=> file hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 240.32 241.58

FILE 'HCAPLUS' ENTERED AT 15:54:19 ON 05 FEB 2008

FILE COVERS 1907 - 5 Feb 2008 VOL 148 ISS 6
FILE LAST UPDATED: 4 Feb 2008 (20080204/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> l6 and l7
            34 L6
            24 L7
L10          1 L6 AND L7

=> l6 and l8
            34 L6
             1 L8
L11          1 L6 AND L8

=> l6 and l9
            34 L6
             1 L9
L12          1 L6 AND L9

=> l10 and l11 and l12
L13          1 L10 AND L11 AND L12

=> d ibib abs hitstr

L13  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2005:14172  HCAPLUS
DOCUMENT NUMBER:         142:114047
TITLE:                   A preparation of furofuranyl derivative, useful as
                         inhibitor of HIV aspartyl protease
INVENTOR(S):             Roberts, John Charles; Toczko, Jennifer Fell
PATENT ASSIGNEE(S):      SmithKline Beecham Corporation, USA; Martin, Michael
                         Tolar
SOURCE:                  PCT Int. Appl., 36 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2005000249         A2    20050106    WO 2004-US20353         20040625
     WO 2005000249         A3    20050407
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
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IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR						
JP 2007521277	T	20070802	JP 2006-517643			20040625
US 2006148865	A1	20060706	US 2005-560500			20051212
PRIORITY APPLN. INFO.:			US 2003-483002P		P	20030627
			WO 2004-US20353		W	20040625

OTHER SOURCE(S): CASREACT 142:114047
GI

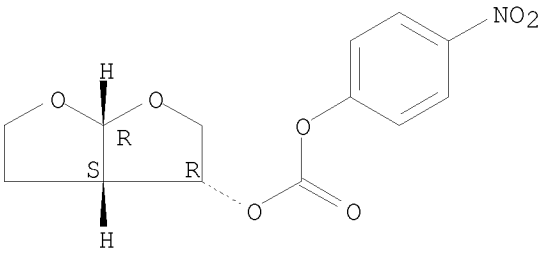
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of furofuranyl derivative I, useful as inhibitor of HIV aspartyl protease (no biol. data). For instance, I was prepared via deprotection of II and coupling with III with a yield of 90% (example 2).

IT 192725-55-6P 820250-08-6P 820250-09-7P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)

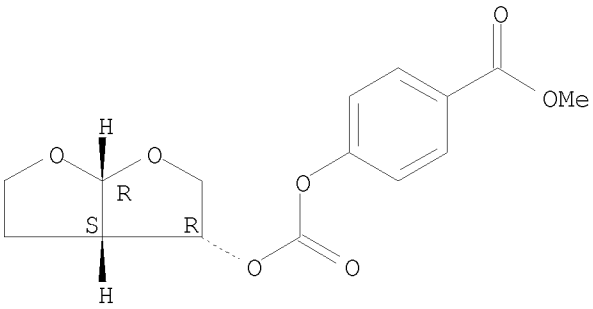
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



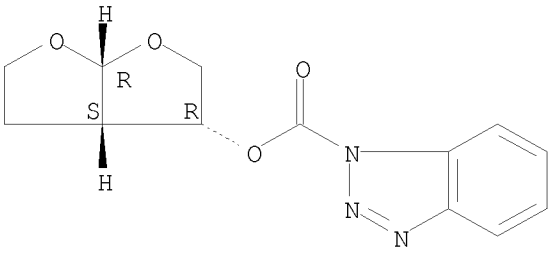
RN 820250-08-6 HCAPLUS
CN Benzoic acid, 4-[[[[(3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl]oxy]carbonyl]oxy]-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



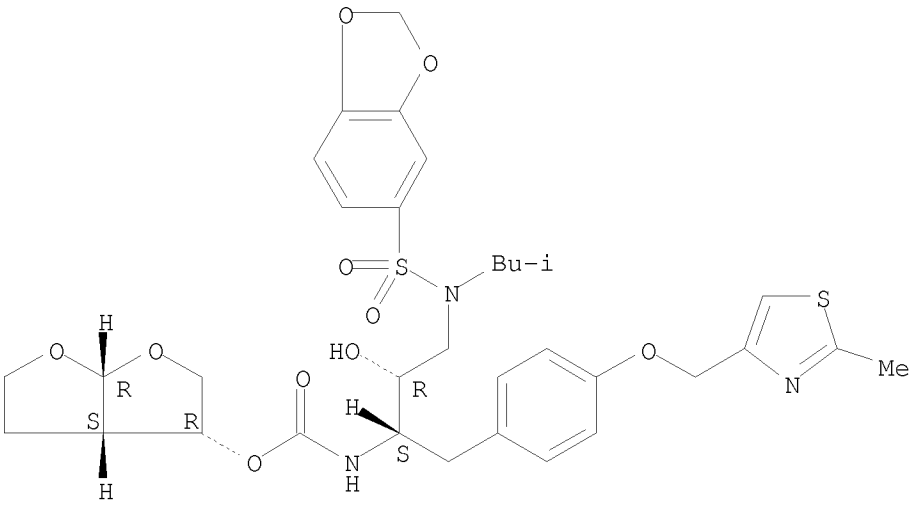
RN 820250-09-7 HCAPLUS
CN 1H-Benzotriazole-1-carboxylic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



IT 313682-08-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)
RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	10.83	252.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE -0.80 -0.80

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:55:14 ON 05 FEB 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJRK1626

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'HCAPLUS' AT 15:59:52 ON 05 FEB 2008
FILE 'HCAPLUS' ENTERED AT 15:59:52 ON 05 FEB 2008
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COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 10.83 252.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY TOTAL SESSION
CA SUBSCRIBER PRICE -0.80 -0.80

=> l6
L14 34 L6

=> l7
L15 24 L7

=> d ibib abs hitstr 1-34

L15 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1275513 HCAPLUS
DOCUMENT NUMBER: 147:502340
TITLE: Process for preparation of carbamic acid bisfuranyl esters as HIV protease inhibitors and their use in the treatment of retroviral infection
INVENTOR(S): Crawford, Kenneth R.; Dowdy, Eric D.; Gutierrez, Arnold; Polniaszek, Richard P.; Yu, Richard Hung Chiu
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2007126812 A2 20071108 WO 2007-US7564 20070329
WO 2007126812 A3 20071221
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
US 2008004242 A1 20080103 US 2007-729522 20070329
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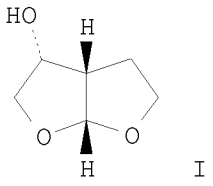
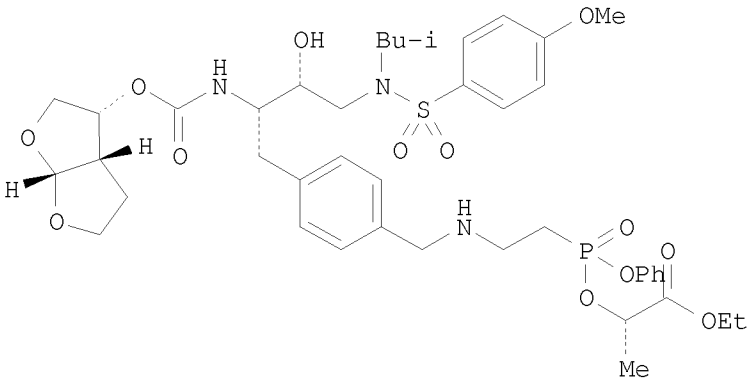
GI



I



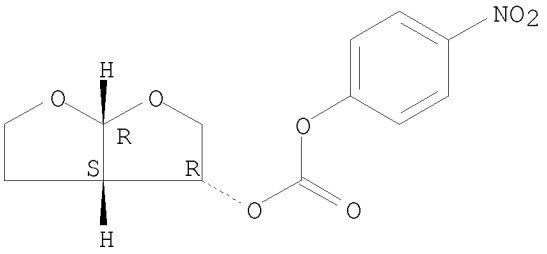
II

AB A process for the synthesis of bisfuran intermediates, e.g., I useful for preparing antiviral HIV protease inhibitor compds. is hereby disclosed. Example compound II was prepared as adipic acid salt and succinic acid salts, using intermediate I as the key component in the preparation The invention compds. were evaluated for their HIV protease inhibitory activity (no data).

IT 192725-55-6P
RL: BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbamic acid bisfuranyl ester compds. as HIV protease inhibitors useful in treatment and prevention of retroviral infection)

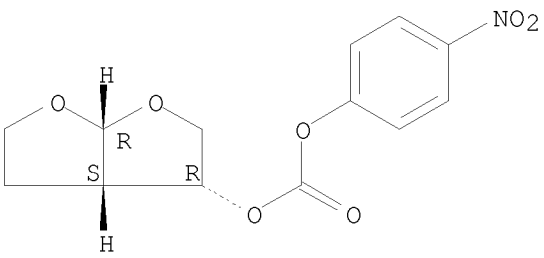
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1131417 HCAPLUS
DOCUMENT NUMBER: 148:33642
TITLE: Research and Development of an Efficient Synthesis of Hexahydrofuro[2,3-b]furan-3-ol Moiety-A Key Component of the HIV Protease Inhibitor Candidates
AUTHOR(S): Yu, Richard H.; Polniaszek, Richard P.; Becker, Mark W.; Cook, Charles M.; Yu, Lok Him L.
CORPORATE SOURCE: Process Research Department, Gilead Sciences, Inc., Foster City, CA, 94404, USA
SOURCE: Organic Process Research & Development (2007), 11(6), 972-980
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 148:33642
AB A highly efficient method for the synthesis of racemic hexahydrofuro[2,3-b]furan-3-ol has been developed utilizing a lanthanide catalyst, such as Yb(fod)3, to promote condensation of 2,3-dihydrofuran and glycolaldehyde dimer. Access to either optically enriched enantiomer of bisfuran alc. can be obtained by using this method employing chiral ligands with the lanthanide catalyst. This method has been demonstrated to be a robust and scalable process with potential application for the construction of a variety of furo[2,3-b]furan derivs.
IT 192725-55-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

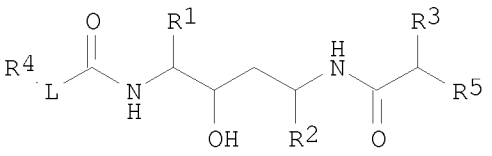


REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:449362 HCAPLUS
DOCUMENT NUMBER: 145:8179
TITLE: Process for the preparation of pyrimidinyl aminodiphenylhexane derivatives as retroviral protease inhibiting prodrugs
INVENTOR(S): Kumar, Gondi N.; Herrin, Thomas R.; Kempf, Dale J.; Betebenner, David A.; Chen, Xiaoqi; Norbeck, Daniel W.; Sham, Hing Leung; Patel, Ketan M.; Liu, Jih-Hua; Tien, Jieh-Heh J.; Stoner, Eric J.; Stengel, Peter J.; Plata, Daniel J.; Oliver, Patricia A.; Kolaczkowski, Lawrence; Hannick, Steven M.; Dickman, Daniel A.; Cooper, Arthur J.; Condon, Stephen L.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Aust. Pat. Appl., 252 pp.
CODEN: AUXXCM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 2004201149	A1	20040422	AU 2004-201149	20040318
AU 2004201149	B2	20070802		
AU 2007231810	A1	20071129	AU 2007-231810	20071101
PRIORITY APPLN. INFO.:			AU 2001-13690 A3	20010112
			AU 2004-201149 A3	20040318

OTHER SOURCE(S): MARPAT 145:8179
GI



I

AB Pyrimidinyl aminodiphenylhexane derivs. I, wherein R1 and R2 are independently lower alkyl, cycloalkyl-alkyl, aryl-alkyl; R3 is lower

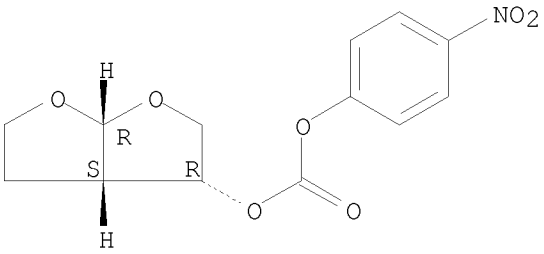
alkyl, cycloalkyl-alkyl, hydroxy-alkyl; R4 is aryl, heterocyclic; R5 is five- or six-membered heterocycle containing at least one nitrogen atom; L is O, S, NH, N-alkyl, , N-cycloalkyl, N-cycloalkyl-alkyl, O-alkylenyl, SO-alkylenyl, S(O)2-alkylenyl, alkylenyl-O, alkylenyl-S, alkylenyl, alkenylenyl, were prepared and tested in vitro and in human as retroviral protease inhibiting prodrugs. Thus, (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-[2S-(1-tetrahydropyrimid-2-onyl)-3-methylbutanoyl]amino-1,6-diphenylhexane was prepared via coupling of (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-amino-1,6-diphenylhexane with 2S-(1-tetrahydro-pyrimid-2-onyl)-3-methylbutanoic acid. The present invention relates to novel compds. and a composition and method for inhibiting retroviral proteases and in particular for inhibiting human immunodeficiency virus (HIV) protease, a composition and method for inhibiting a retroviral infection and in particular an HIV infection, processes for making the compds. and synthetic intermediates employed in the processes. While the compound of the invention can be administered as the sole active pharmaceutical agent, it can also be used in combination with one or more immunomodulators, antiviral agents, other antiinfective agents, or vaccines. The compds. of the invention are useful for inhibiting retroviral protease, in particular HIV protease, in vitro or in vivo (especially in mammals and in particular in humans). Total daily dose administered to a human or other mammal host in single or divided doses may be in amts., for example, from 0.001 to 300 mg/kg body weight daily and more usually 0.1 to 20 mg/kg body weight daily.

IT 192725-55-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of pyrimidinyl aminodiphenylhexane derivs. as retroviral protease inhibiting prodrugs)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1154569 HCAPLUS

DOCUMENT NUMBER: 143:406046

TITLE: Preparation of azacyclosteroids as histamine-3 receptor ligands

PATENT ASSIGNEE(S): Abbott Laboratories, USA; Zhao, Chen; Sun, Minghua; Cowart, Marlon D.; Bennani, Youssef L.

SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005100377	A1	20051027	WO 2005-US14019	20050406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005245495	A1	20051103	US 2004-819849	20040407
CA 2562189	A1	20051027	CA 2005-2562189	20050406
EP 1735332	A1	20061227	EP 2005-738987	20050406
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007532583	T	20071115	JP 2007-507579	20050406
MX 2006PA11669	A	20070123	MX 2006-PA11669	20061006
PRIORITY APPLN. INFO.:			US 2004-819849 A	20040407
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OTHER SOURCE(S): CASREACT 143:406046; MARPAT 143:406046
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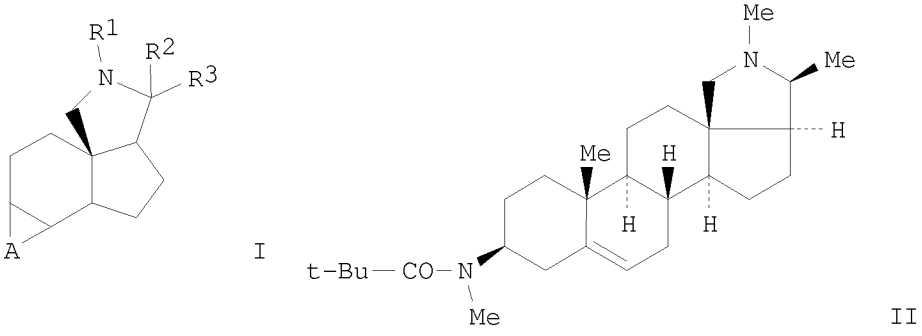
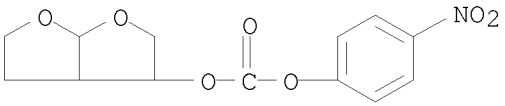


AB Azacyclosteroids of formula I [R1 = H, acetyl, alkyl, fluoroalkyl, cycloalkyl; R2, R3 = H, alkyl; R2R3 = 3-6 membered ring; A = (substituted) benzo or naphthyl fused ring] are prepared as histamine H3 receptor ligands. Thus, II was prepared starting from conessine. Representative compds. had binding affinities between 810 nM to 0.12 nM.

IT 854745-99-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of azacyclosteroids as histamine H3 receptor ligands)

RN 854745-99-6 HCAPLUS
CN Carbonic acid, hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1154157 HCAPLUS
DOCUMENT NUMBER: 143:422465
TITLE: Preparation of phosphonate analogs of HIV protease inhibitors and methods for identifying anti-HIV therapeutic compounds
INVENTOR(S): Arimilli, Murty N.; Becker, Mark M.; Birkus, Gabriel
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 1034 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005239054	A1	20051027	US 2003-740694	20031222
WO 2003090690	A2	20031106	WO 2003-US12901	20030425
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WO 2003091264	A3	20040311		
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     US 2005197320         A1    20050908    US 2003-424130          20030425
     US 2005209197         A1    20050922    US 2003-423496          20030425
     CN 101041669          A     20070926    CN 2006-10154203        20030425
     CN 101074242          A     20071121    CN 2007-10085746        20030425
     ZA 2004009376         A     20050914    ZA 2004-9376            20041122
     ZA 2004009377         A     20060329    ZA 2004-9377            20041122
     AU 2004309379         A1    20050714    AU 2004-309379          20041222
     CA 2550730            A1    20050714    CA 2004-2550730         20041222
     WO 2005064008         A1    20050714    WO 2004-US42991         20041222
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PRIORITY APPLN. INFO.:                       US 2002-375622P     P   20020426
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                                             US 2003-423496      A2  20030425
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                                             US 2003-424186      A2  20030425
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                                             US 2003-465824P     P   20030425
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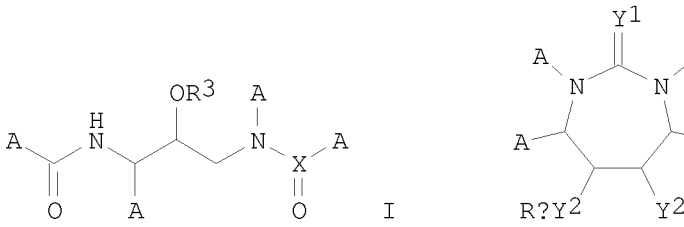

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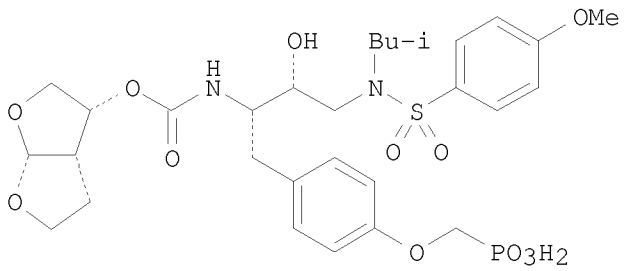


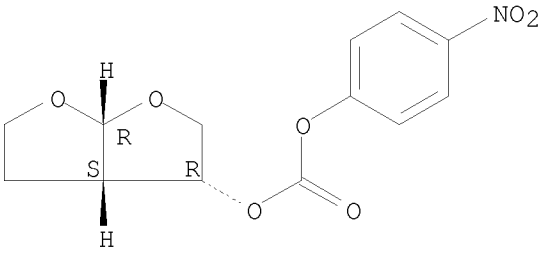
III

AB The invention relates to phosphonate-substituted carbamates I and cyclic ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SO0-2, or SO0-2SO0-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, S0-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Compds. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Libraries of such compds. were screened optionally using the novel enzyme GS-7340 ester hydrolase. Compns. and methods relating to GS-7340 ester hydrolase also are provided. Examples include prepns. for non-nucleoside phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (Ki ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1106795 HCAPLUS
DOCUMENT NUMBER: 143:367448
TITLE: Preparation of azacyclosteroid histamine-3 receptor ligands
INVENTOR(S): Zhao, Chen; Sun, Minghua; Cowart, Marlon D.; Bennani, Youssef L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 85 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005227953	A1	20051013	US 2005-96382		20050401
PRIORITY APPLN. INFO.:			US 2004-560151P	P	20040407

OTHER SOURCE(S): MARPAT 143:367448
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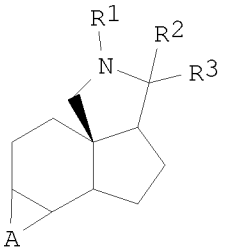

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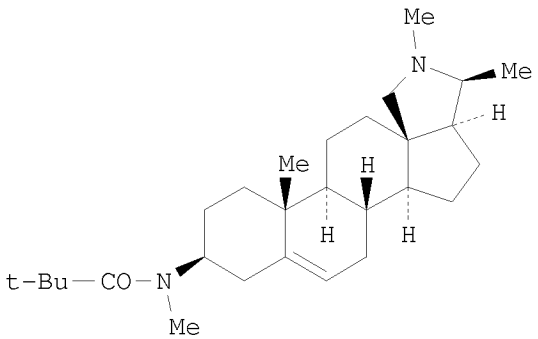


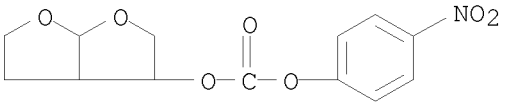
II

AB Azacyclosteroids of formula I [R1 = H, acetyl, alkyl, fluoroalkyl, cycloalkyl; R2, R3 = H, alkyl; R2R3 = 3-6-membered ring; A = fused (substituted) naphthyl or benzo ring] are prepared as histamine H2 receptor ligands. Thus, II was prepared starting from conessine. The compds. had binding affinities from about 810 nM to 0.12 nM against histamine-3 receptor.

IT 854745-99-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of azacyclosteroids as histamine H3 receptor ligands)

RN 854745-99-6 HCAPLUS

CN Carbonic acid, hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)



L15 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:612479 HCAPLUS

DOCUMENT NUMBER: 143:97530

TITLE: Preparation of phosphonate analogs of HIV protease inhibitors and methods for identifying anti-HIV therapeutic compounds

INVENTOR(S): Arimilli, Murty N.; Becker, Mark M.; Birkus, Gabriel; Bryant, Clifford; Chen, James M.; Chen, Xiaowu; Cihlar, Tomas; Dastgah, Azar; Eisenberg, Eugene J.; Fardis, Maria; Hatada, Marcos; He, Gong-Xin; Jin, Haolun; Kim, Choung U.; Lee, William A.; Lee, Christopher P.; Lin, Kuei-Ying; Liu, Hongtao; Mackman, Richard L.; McDermott, Martin J.; Mitchell, Michael L.; Nelson, Peter H.; Pyun, Hyung-Jung; Rowe, Tanisha D.; Sparacino, Mark; Swaminathan, Sundaramoorthi; Tario, James D.; Wang, Jianying; Williams, Matthew A.; Xu, Lianhong; Yang, Zheng-Yu; Yu, Richard H.; Zhang, Jiancun; Zhang, Lijun

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 1723 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005064008	A1	20050714	WO 2004-US42991	20041222
WO 2005064008	A9	20060928		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

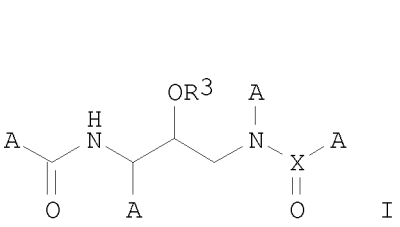
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

US 2005239054	A1	20051027	US 2003-740694		20031222
AU 2004309379	A1	20050714	AU 2004-309379		20041222
CA 2550730	A1	20050714	CA 2004-2550730		20041222
EP 1711617	A1	20061018	EP 2004-817046		20041222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS					
JP 2007515184	T	20070614	JP 2006-547281		20041222

PRIORITY APPLN. INFO.:

US 2003-740694	A	20031222
US 2002-375622P	P	20020426
US 2002-375665P	P	20020426
US 2002-375779P	P	20020426
US 2002-375834P	P	20020426
US 2003-423496	A2	20030425
US 2003-424130	A2	20030425
US 2003-424186	A2	20030425
US 2003-465721P	P	20030425
US 2003-465810P	P	20030425
US 2003-465824P	P	20030425
WO 2003-US12901	A2	20030425
WO 2003-US12926	A2	20030425
WO 2003-US12943	A2	20030425
WO 2004-US42991	W	20041222

GI



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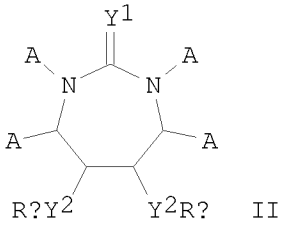

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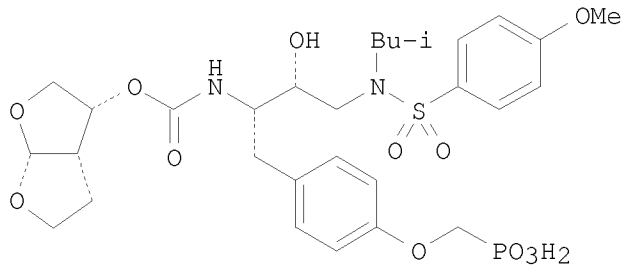


III

AB The invention relates to phosphonate-substituted carbamates I and cyclic ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of

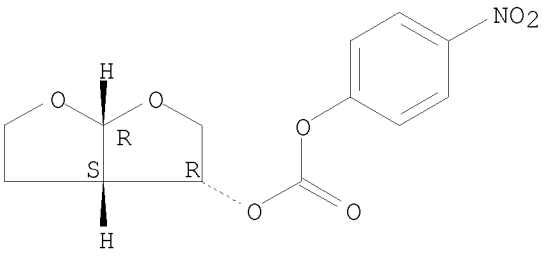
A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SO0-2, or SO0-2SO0-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, S0-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Compds. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Libraries of such compds. were screened optionally using the novel enzyme GS-7340 ester hydrolase. Compns. and methods relating to GS-7340 ester hydrolase also are provided. Examples include prepns. for non-nucleoside phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (Ki ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:589363 HCAPLUS
DOCUMENT NUMBER: 143:248118
TITLE: Synthesis and antiviral activities of novel

N-alkoxy-arylsulfonamide-based HIV protease inhibitors

AUTHOR(S): Sherrill, Ronald G.; Furfine, Eric S.; Hazen, Richard J.; Miller, John F.; Reynolds, David J.; Sammond, Douglas M.; Spaltenstein, Andrew; Wheelan, Pat; Wright, Lois L.

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(15), 3560-3564
CODEN: BMCLE8; ISSN: 0960-894X

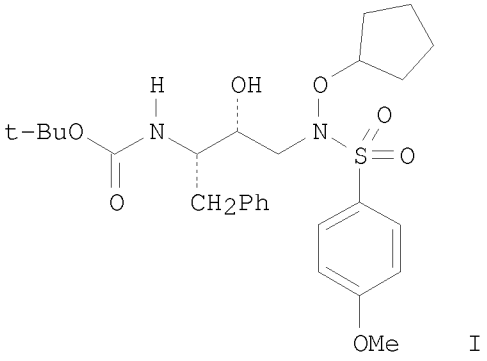
PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:248118

GI



I

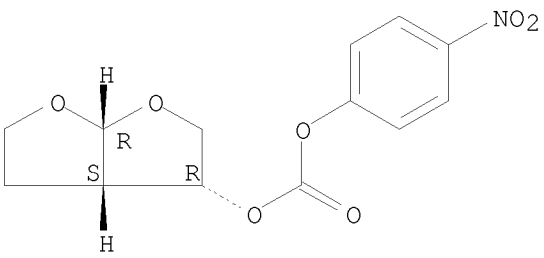
AB A series of N-alkoxy-arylsulfonamide HIV protease inhibitors, e.g., I, with low picomolar enzyme activity and single digit nanomolar antiviral activity is disclosed.

IT 192725-55-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, antiviral activity, HIV protease inhibitory activity, and structure-activity relationship of N-alkoxy arylsulfonamide derivs. starting from alkoxyamines, phenylalanine-epoxide, and arylsulfonyl chlorides)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

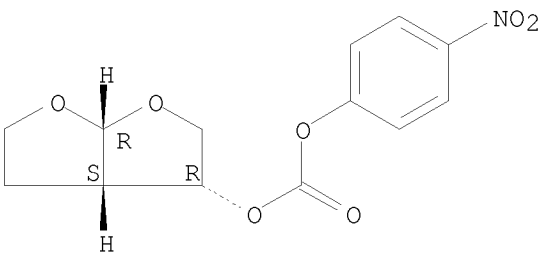
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:589326 HCAPLUS
DOCUMENT NUMBER: 143:267225
TITLE: Novel P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles
AUTHOR(S): Miller, John F.; Brieger, Michael; Furfine, Eric S.; Hazen, Richard J.; Kaldor, Istvan; Reynolds, David; Sherrill, Ronald G.; Spaltenstein, Andrew
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(15), 3496-3500
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:267225
AB A novel series of tyrosine-derived HIV protease inhibitors was synthesized and evaluated for in vitro antiviral activity against wild-type virus and two protease inhibitor-resistant viruses. All of the compds. had wild-type antiviral activities that were similar to or greater than several currently marketed HIV protease inhibitors. In addition, a number of compds. in this series were more potent against the drug-resistant mutant viruses than they were against wild-type virus.
IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

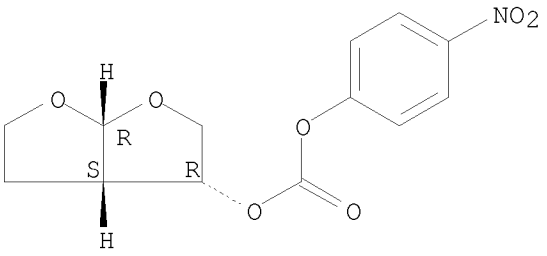
L15 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:588404 HCAPLUS
DOCUMENT NUMBER: 143:133693
TITLE: Preparation of amino acid derivatives as HIV protease inhibitors
INVENTOR(S): Degoey, David A.; Flentge, Charles A.; Flosi, William J.; Grampovnik, David J.; Kempf, Dale J.; Klein, Larry L.; Yeung, Ming C.; Randolph, John T.; Wang, Xiu C.; Yu, Su
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 279 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005148623	A1	20050707	US 2004-8713		20041209
PRIORITY APPLN. INFO.:			US 2003-528974P	P	20031211

OTHER SOURCE(S): MARPAT 143:133693
AB The invention relates to amino acid derivs. A-NHCHR6CHR5CHR4CHR3NHCOCHR2NHCO2R1 [A is an amino acid or acyl residue of defined structure; R1, R2, R3, R6 are independently (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl or heteroaryl; R4, R5 are H (not both), OH or substituted hydroxyl], including pharmaceutically-acceptable salts, prodrugs or stereoisomers, having HIV protease inhibitory activity. Thus, Me (1S,4R,6S,7S,10S)-7-benzyl-1,10-di-tert-butyl-6-hydroxy-2,9,12-trioxo-4-[4-(2-pyridinyl)benzyl]-13-oxa-3,8,11-triazatetradec-1-ylcarbamate was prepared by a multistep procedure, which includes the reaction of intermediate tert-Bu (1S,2S,4R)-4-amino-1-benzyl-2-hydroxy-5-[4-(2-pyridinyl)phenyl]pentylcarbamate with N-protected L-tert-leucine. Compds. of the invention showed EC50 values in the range 0.7 nM to >3.2 μM against wild-type HIV.
IT 192725-55-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as HIV protease inhibitors)
RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:527407 HCAPLUS
DOCUMENT NUMBER: 143:59982
TITLE: Preparation of HIV protease inhibitors, in particular imidazolidine derivatives
INVENTOR(S): Flentge, Charles A.; Chen, Hui-Ju; Degoey, David A.; Flosi, William J.; Grampovnik, David J.; Huang, Peggy P.; Kempf, Dale J.; Klein, Larry L.; Krueger, Allan C.; Madigan, Darold L.; Randolph, John T.; Sun, Minghua; Yeung, Ming C.; Zhao, Chen
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 287 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005131042	A1	20050616	US 2003-733915	20031211
CA 2549389	A1	20050707	CA 2004-2549389	20041110
WO 2005061450	A2	20050707	WO 2004-US37745	20041110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1709037	A2	20061011	EP 2004-810802	20041110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
JP 2007513944	T	20070531	JP 2006-543826	20041110
MX 2006PA06610	A	20060831	MX 2006-PA6610	20060609

PRIORITY APPLN. INFO.: US 2003-733915 A 20031211

WO 2004-US37745 W 20041110

OTHER SOURCE(S): MARPAT 143:59982
GI

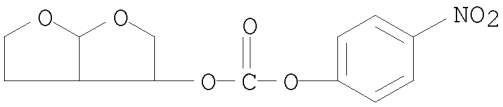
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. of formula ANH(CHR)(CHR1)(CHR2)NR3S(O2)R4 (I) [wherein A = alkylcarbonyl, arylsulfonyl, 1,3-substituted 2-oxoimidazolidinyl, 2,4-dioxoimidazolidinyl, etc.; X, Y = independently O, S, NH; R = (un)substituted alk(en)yl, cycloalk(en)yl, hetero/arylalkyl, etc.; R1 = OH and derivs., OPO3H and derivs., OSO2H and derivs., etc.; R2 = H; R3 = halo/alkyl, halo/alkenyl, (un)substituted cycloalk(en)yl, aryl; R4 = (un)substituted cycloalk(en)yl, heterocyclyl, hetero/aryl] were prepared as HIV protease inhibitors. For example, II was prepared, in 62% yield, by coupling acid III (preparation given) with amine IV (preparation given). I showed antiviral activity against Wild-Type HIV with EC50 in the range of 1 nM to 100 nM.

IT 854745-99-6P, Hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl carbonate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of HIV protease inhibitors, in particular imidazolidine derivs.)

RN 854745-99-6 HCAPLUS

CN Carbonic acid, hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)



L15 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:527398 HCAPLUS
DOCUMENT NUMBER: 143:78485
TITLE: Preparation of amino acid derivatives as HIV protease inhibitors
INVENTOR(S): Degoey, David A.; Flentge, Charles A.; Flosi, William J.; Grampovnik, David J.; Kempf, Dale J.; Klein, Larry L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 204 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2005131017 A1 20050616 US 2003-733946 20031211
CA 2549098 A1 20050630 CA 2004-2549098 20041209
WO 2005058841 A2 20050630 WO 2004-US41658 20041209
WO 2005058841 A3 20060309
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1697344 A2 20060906 EP 2004-813910 20041209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU
JP 2007516260 T 20070621 JP 2006-544070 20041209
MX 2006PA06612 A 20060831 MX 2006-PA6612 20060609
PRIORITY APPLN. INFO.: US 2003-733946 A 20031211
WO 2004-US41658 W 20041209
OTHER SOURCE(S): CASREACT 143:78485; MARPAT 143:78485

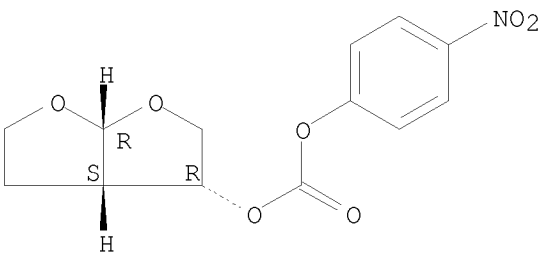
AB The invention relates to amino acid derivs. A-NHCHR6CHR5CHR4CHR3NHCOCHR2NHCO2R1 [A is an amino acid or acyl residue of defined structure; R1, R2, R3, R6 are independently (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl or heteroaryl; R4, R5 are H (not both), OH or substituted hydroxyl], including pharmaceutically-acceptable salts, stereoisomers, esters or prodrugs, having HIV protease inhibitory activity. Thus, Me (1S,4R,6S,7S,10S)-7-benzyl-1,10-di-tert-butyl-6-hydroxy-2,9,12-trioxo-4-[4-(2-pyridinyl)benzyl]-13-oxa-3,8,11-triazatetradec-1-ylcarbamate was prepared by a multistep procedure, which includes the reaction of intermediate tert-Bu (1S,2S,4R)-4-amino-1-benzyl-2-hydroxy-5-[4-(2-pyridinyl)phenyl]pentylcarbamate with N-protected L-tert-leucine. Compds. of the invention showed EC50 values 0.7-300 nM against wild-type HIV.

IT 192725-55-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as HIV protease inhibitors)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:14172 HCAPLUS
DOCUMENT NUMBER: 142:114047
TITLE: A preparation of furofuranyl derivative, useful as inhibitor of HIV aspartyl protease
INVENTOR(S): Roberts, John Charles; Toczko, Jennifer Fell
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; Martin, Michael Tolar
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005000249	A2	20050106	WO 2004-US20353		20040625
WO 2005000249	A3	20050407			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1638960	A2	20060329	EP 2004-777060		20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR					
JP 2007521277	T	20070802	JP 2006-517643		20040625
US 2006148865	A1	20060706	US 2005-560500		20051212
PRIORITY APPLN. INFO.:			US 2003-483002P	P	20030627
			WO 2004-US20353	W	20040625

OTHER SOURCE(S): CASREACT 142:114047
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

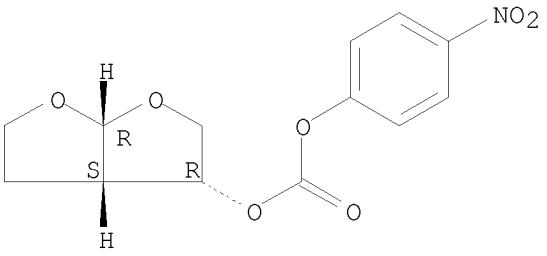
AB The invention relates to a preparation of furofuranyl derivative I, useful as inhibitor of HIV aspartyl protease (no biol. data). For instance, I was prepared via deprotection of II and coupling with III with a yield of 90% (example 2).

IT 192725-55-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:534173 HCAPLUS

DOCUMENT NUMBER: 141:89016

TITLE: Preparation of benzimidazolylazabicyclooctylethylpiperidines as Ccr5 antagonists for the treatment of HIV infection

INVENTOR(S): Kazmierski, Wieslaw Mieczyslaw; Aquino, Christopher Joseph; Bifulco, Neil; Boros, Eric Eugene; Chauder, Brian Andrew; Chong, Pek Yoke; Duan, Maosheng; Deanda, Felix, Jr.; Koble, Cecilia Suarez; Mclean, Ed Williams; Peckham, Jennifer Poole; Perkins, Angilique C.; Thompson, James Benjamin; Vanderwall, Dana

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; et al.; et al.

SOURCE: PCT Int. Appl., 859 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054974	A2	20040701	WO 2003-US39644	20031212
WO 2004054974	A3	20040902		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,

TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2509711	A1	20040701	CA 2003-2509711		20031212
AU 2003300902	A1	20040709	AU 2003-300902		20031212
EP 1569646	A2	20050907	EP 2003-813419		20031212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003017230	A	20051025	BR 2003-17230		20031212
CN 1744899	A	20060308	CN 2003-80109628		20031212
JP 2006511554	T	20060406	JP 2004-560838		20031212
NO 2005002739	A	20050819	NO 2005-2739		20050607
US 2006229336	A1	20061012	US 2005-538144		20050609
MX 2005PA06354	A	20050826	MX 2005-PA6354		20050613
IN 2005KN01328	A	20060630	IN 2005-KN1328		20050711
ZA 2005005600	A	20060927	ZA 2005-5600		20050712
PRIORITY APPLN. INFO.:			US 2002-433634P	P	20021213
			WO 2003-US39644	W	20031212

OTHER SOURCE(S): MARPAT 141:89016
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. I [R1 = (optionally substituted) alkyl, aryl, heteroaryl, carbocyclyl; R2 = H, (optionally substituted) alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroarylalkyl, heteroarylcycloalkyl, aralkylcarbonyl, heteroarylsulfinyl; R3 = H, halo, cyano, trifluoromethyl, (optionally substituted) amino, acylamino, alkyl; X = C1-5 alkylene, optionally substituted with oxo or thioxo groups or halogen atoms, and optionally containing 1-3 oxygen, nitrogen, sulfur, or phosphorus atoms; Y = carbonyl, thiocarbonyl, 1,2-dioxoethylene, oxyalkylcarbonyl, sulfinyl, sulfonyl, oxycyanoimino, (optionally substituted) aminocarbonyl, carbonylamino, aminothiocarbonyl, oxyiminomethyl, thioiminomethyl, amino(cyanoimino)methyl, (cyanoimino)methyl, amino(acylimino)methyl, amino(sulfonylimino)methyl, amino(sulfinylimino)methyl, amino(alkoxyimino)methyl, amino(imino)methyl, (cyanoimino)methoxy, iminomethoxy, (cyanoimino)methanethiyl, alkylcarbonyloxy; A = saturated, partially saturated, or aromatic monocyclic ring with 5-6 atoms or a bicyclic ring with 8-10 members containing 0-5 nitrogen, oxygen, and/or sulfur atoms] such as II are prepared I are prepared as Ccr5 antagonists for the treatment of viral infections, (particularly HIV infection), related syndromes such as AIDS-related complex (ARC), progressive generalized lymphadenopathy, Kaposi's sarcoma, and neurol. conditions, and other diseases such as multiple sclerosis, rheumatoid arthritis, Crohn's disease, and immune-mediated disorders. The invention compds. have pIC50 values of ≥5 in assays for Ccr5 antagonism. Piperidineacetaldehyde III is prepared in four steps from 4-phenyl-4-piperidinecarbonitrile by protection of the piperidine with Boc anhydride, reduction of the nitrile with diisobutylaluminum hydride, Wittig olefination with methoxymethylphosphonium chloride, and hydrolysis of the enol ether with catalytic p-toluenesulfonic acid monohydrate. The

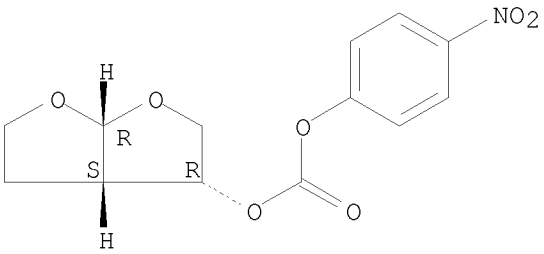
hydrochloride of endo-(benzimidazolyl)azabicyclooctane IV is prepared in five steps from tert-Bu endo-3-oxo-8-azabicyclo[3.2.1]octane-8-carboxylate; reductive amination with benzylamine, reductive cleavage of the benzyl group by palladium-mediated hydrogenation, a nucleophilic aryl substitution reaction with 1-fluoro-2-nitrobenzene, reduction of the nitro group by hydrogenation over palladium on carbon, and treatment with tri-Et orthoacetate followed by treatment with hydrochloric acid in ethanol. Coupling of III and IV by reductive amination with sodium triacetoxyborohydride, cleavage of the Boc group with hydrochloric acid in dioxane, and acylation with pivaloyl chloride and triethylamine yields II.

IT 192725-55-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of benzimidazolylazabicyclooctylethylpiperidine Ccr5 antagonists in the treatment of bacterial and viral infections and other diseases)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:99287 HCAPLUS

DOCUMENT NUMBER: 140:339141

TITLE: Novel arylsulfonamides possessing sub-picomolar HIV protease activities and potent anti-HIV activity against wild-type and drug-resistant viral strains

AUTHOR(S): Miller, John F.; Furfine, Eric S.; Hanlon, Mary H.; Hazen, Richard J.; Ray, John A.; Robinson, Laurence; Samano, Vicente; Spaltenstein, Andrew

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(4), 959-963
CODEN: BMCLE8; ISSN: 0960-894X

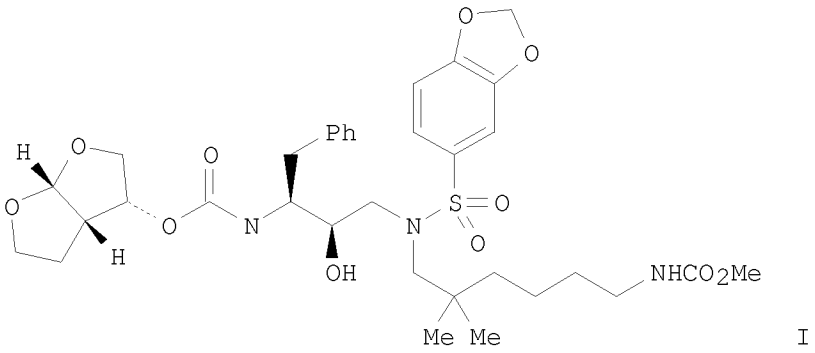
PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:339141

GI



I

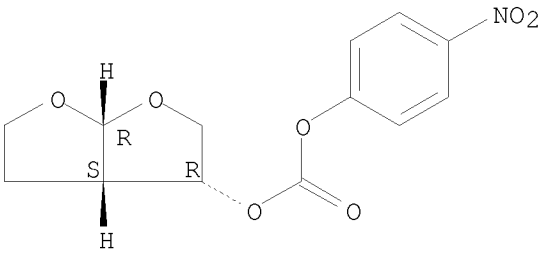
AB Furanofuryl analogs of the HIV protease inhibitor amprenavir such as I are prepared in which a terminally substituted n-alkyl group is appended to the N-iso-Bu group of amprenavir and in which the substituents on the N-arylsulfonyl moiety are varied. Some of the inhibitors such as I are found to have greatly enhanced inhibition of HIV protease; the amprenavir analogs also inhibit the growth of both wild-type and resistant strains of HIV and are more effective against the HIV strains than the currently marketed HIV protease inhibitors amprenavir, indinavir, and nelfinavir. E.g., I inhibits wild-type HIV protease with a Ki value of 0.014 pM, and inhibits wild-type and resistant strains of HIV with IC50 values of between 1.6 nM and 15 nM.

IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of furanofuryl amprenavir analogs with modifications at the N-arylsulfonyl and N-iso-Bu moieties which show improved HIV protease inhibition and inhibition of wild-type and resistant HIV strains)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:875072 HCAPLUS
DOCUMENT NUMBER: 139:381610
TITLE: Preparation of phosphonate analogs of HIV protease

inhibitors and methods for identifying anti-HIV therapeutic compounds

INVENTOR(S): Birkus, Gabriel; Chen, James M.; Chen, Xiaowu; Cihlar, Tomas; Eisenberg, Eugene J.; Hatada, Marcos; He, Gong-Xin; Kim, Choung U.; Lee, William A.; McDermott, Martin J.; Swaminathan, Sundaramoorthi

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 814 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090691	A2	20031106	WO 2003-US12943	20030425
WO 2003090691	A3	20060209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2481449	A1	20031106	CA 2003-2481449	20030425
AU 2003228707	A1	20031110	AU 2003-228707	20030425
CN 1649885	A	20050803	CN 2003-814963	20030425
CN 1656109	A	20050817	CN 2003-812478	20030425
EP 1575486	A2	20050921	EP 2003-726472	20030425
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JP 2006508634	T	20060316	JP 2003-587330	20030425
AT 367394	T	20070815	AT 2003-747326	20030425
CN 101041669	A	20070926	CN 2006-10154203	20030425
CN 101074242	A	20071121	CN 2007-10085746	20030425
WO 2004096818	A2	20041111	WO 2003-EP12423	20031106
WO 2004096818	A3	20050407		
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AU 2003291998	A1	20041123	AU 2003-291998	20031106
EP 1620445	A2	20060201	EP 2003-767521	20031106
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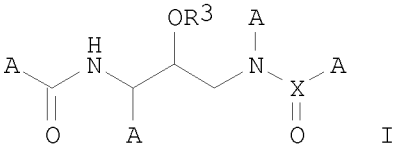
JP 2006524487	T	20061102	JP 2004-571244	20031106
US 2005239054	A1	20051027	US 2003-740694	20031222

US 2005136397	A1	20050623	US 2004-970389		20041022
US 7273716	B2	20070925			
ZA 2004009376	A	20050914	ZA 2004-9376		20041122
ZA 2004009377	A	20060329	ZA 2004-9377		20041122
US 2006115815	A1	20060601	US 2005-511183		20050223
US 2007190523	A1	20070816	US 2007-554287		20070212
PRIORITY APPLN. INFO.:			US 2002-375622P	P	20020426
			US 2002-375665P	P	20020426
			US 2002-375779P	P	20020426
			US 2002-375834P	P	20020426
			CN 2003-812478	A3	20030425
			CN 2003-814963	A3	20030425
			US 2003-423496	A2	20030425
			US 2003-424130	A2	20030425
			US 2003-424186	A2	20030425
			US 2003-465721P	P	20030425
			US 2003-465810P	P	20030425
			US 2003-465824P	P	20030425
			WO 2003-US12901	A	20030425
			WO 2003-US12926	A	20030425
			WO 2003-US12943	W	20030425
			US 2003-513532P	P	20031024
			US 2003-513542P	P	20031024
			US 2003-514241P	P	20031024
			US 2003-514299P	P	20031024
			US 2003-514894P	P	20031029
			US 2003-514925P	P	20031029
			WO 2003-EP12423	W	20031106
			WO 2004-US35083	A	20041022

GI



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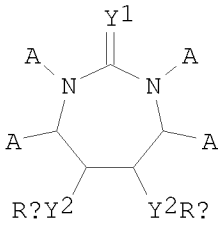
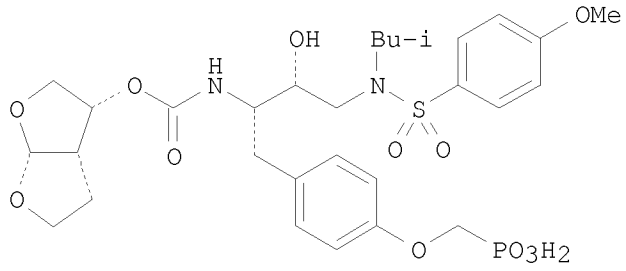


II



III

AB The invention relates to phosphonate-substituted carbamates I and cyclic

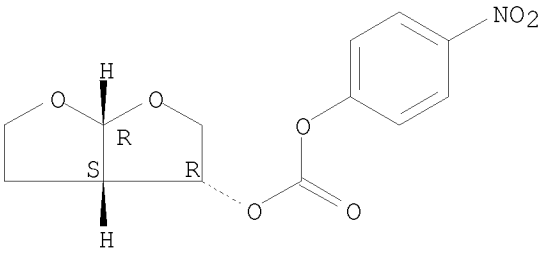
ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SO0-2, or SO0-2SO0-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, S0-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Compds. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Libraries of such compds. were screened optionally using the novel enzyme GS-7340 ester hydrolase. Compns. and methods relating to GS-7340 ester hydrolase also are provided. Examples include prepns. for non-nucleoside phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (Ki ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:875071 HCAPLUS
DOCUMENT NUMBER: 139:381609
TITLE: Preparation of phosphonate analogs of HIV protease inhibitors with improved cellular accumulation

properties

INVENTOR(S): Arimilli, Murty N.; Becker, Mark M.; Bryant, Clifford; Chen, James M.; Chen, Xiaowu; Dastgah, Azar; Fardis, Maria; He, Gong-Xin; Jin, Haolun; Kim, Choung U.; Lee, William A.; Lee, Christopher P.; Lin, Kuei-Ying; Liu, Hongtao; Mackman, Richard L.; Mitchell, Michael L.; Nelson, Peter H.; Pyun, Hyung-Jung; Rowe, Tanisha D.; Sparacino, Mark; Swaminathan, Sundaramoorthi; Tario, James D.; Wang, Jianying; Williams, Matthew A.; Xu, Lianhong; Yang, Zheng-Yu; Yu, Richard H.; Zhang, Jiancun; Zhang, Lijun

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 1727 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

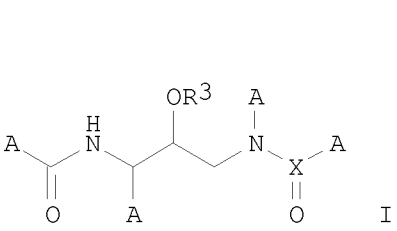
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090690	A2	20031106	WO 2003-US12901	20030425
WO 2003090690	A3	20040624		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2481261	A1	20031106	CA 2003-2481261	20030425
AU 2003231765	A1	20031110	AU 2003-231765	20030425
BR 2003009573	A	20050201	BR 2003-9573	20030425
EP 1509537	A2	20050302	EP 2003-747326	20030425
EP 1509537	B1	20070718		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1649885	A	20050803	CN 2003-814963	20030425
JP 2005523912	T	20050811	JP 2003-587329	20030425
CN 1656109	A	20050817	CN 2003-812478	20030425
AT 367394	T	20070815	AT 2003-747326	20030425
CN 101041669	A	20070926	CN 2006-10154203	20030425
NZ 535828	A	20071026	NZ 2003-535828	20030425
CN 101074242	A	20071121	CN 2007-10085746	20030425
WO 2004096818	A2	20041111	WO 2003-EP12423	20031106
WO 2004096818	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,				

	ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU	2003291998	A1	20041123	AU 2003-291998	20031106
EP	1620445	A2	20060201	EP 2003-767521	20031106
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
JP	2006524487	T	20061102	JP 2004-571244	20031106
US	2005239054	A1	20051027	US 2003-740694	20031222
IN	2004DN03045	A	20070413	IN 2004-DN3045	20041005
MX	2004PA10527	A	20041213	MX 2004-PA10527	20041022
ZA	2004009376	A	20050914	ZA 2004-9376	20041122
ZA	2004009377	A	20060329	ZA 2004-9377	20041122
NO	2004005150	A	20050126	NO 2004-5150	20041125
US	2007010489	A1	20070111	US 2005-511998	20050725
US	2007190523	A1	20070816	US 2007-554287	20070212
PRIORITY APPLN. INFO.:				US 2002-375622P	P 20020426
				US 2002-375665P	P 20020426
				US 2002-375779P	P 20020426
				US 2002-375834P	P 20020426
				CN 2003-812478	A3 20030425
				CN 2003-814963	A3 20030425
				US 2003-423496	A2 20030425
				US 2003-424130	A2 20030425
				US 2003-424186	A2 20030425
				US 2003-465721P	P 20030425
				US 2003-465810P	P 20030425
				US 2003-465824P	P 20030425
				WO 2003-US12901	W 20030425
				WO 2003-US12926	A 20030425
				WO 2003-US12943	A 20030425
				WO 2003-EP12423	W 20031106

OTHER SOURCE(S): MARPAT 139:381609

GI



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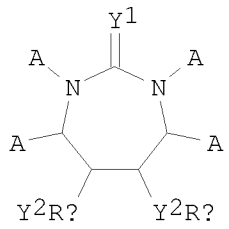

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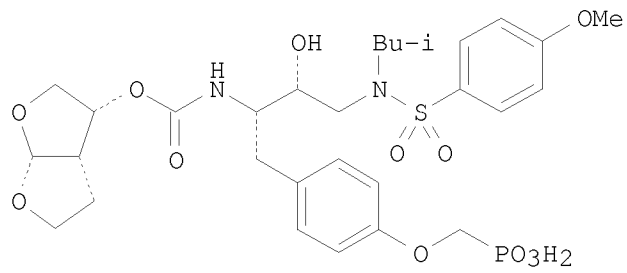


III

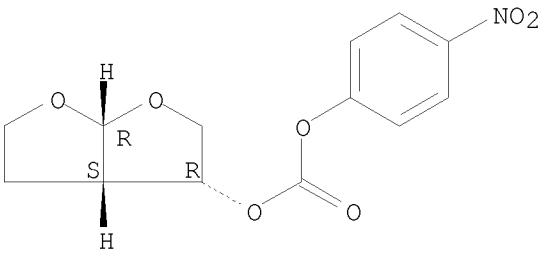
AB The invention relates to phosphonate-substituted carbamates I and cyclic ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SO0-2, or SO0-2SO0-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, S0-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Compds. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Examples include prepns. for non-nucleoside saquinavir-like, lopinavir-like, ritonavir-like, indinavir-like, atazanavir-like, nefinavir-like, tipranavir-like, amprenavir-like, KNI-like, and cyclic carbonyl-like phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (Ki ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



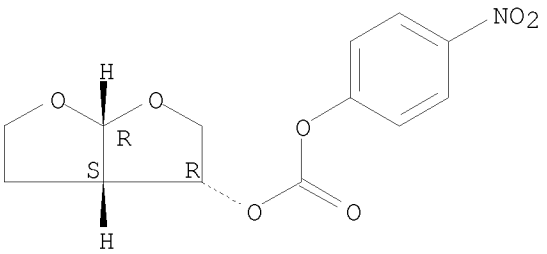
L15 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:795073 HCAPLUS

DOCUMENT NUMBER: 140:41969
TITLE: Synthesis and SAR studies of potent HIV protease inhibitors containing novel dimethylphenoxyl acetates as P2 ligands
AUTHOR(S): Chen, Xiaoqi; Kempf, Dale J.; Li, Lin; Sham, Hing L.; Vasavanonda, Sudthida; Wideburg, Norman E.; Saldivar, Ayda; Marsh, Kennan C.; McDonald, Edith; Norbeck, Daniel W.
CORPORATE SOURCE: Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL, 60064, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(21), 3657-3660
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:41969

AB Iso-Pr substituted 4-thioazolyl valine side chains are highly optimized P2-P3 ligands for C2 symmetry-based HIV protease inhibitors, as exemplified by the drug ritonavir. Replacement of the side chain with the conformationally constrained hexahydrofurofuranyloxy P2 ligand in combination with a dimethylphenoxyacetate on the other end of the ritonavir core diamine yielded highly potent HIV protease inhibitors. The in vitro antiviral activity in MT4 cells increased by 10- and 20-fold, resp., in the absence and presence of 50% human serum compared to ritonavir. The structure-activity relationships of inhibitor series with this combination of ligands were investigated. Preliminary pharmacokinetic studies in rats indicated rapid elimination of the inhibitors from the blood, and the plasma levels were not significantly enhanced by coadministration with ritonavir. However, the novel structural features and the high intrinsic antiviral potency of this series provides potential for the future exploration of prodrug strategies.

IT 192725-55-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structure-activity relationship of potent HIV protease inhibitor containing novel dimethylphenoxyl acetates as P2 ligands)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



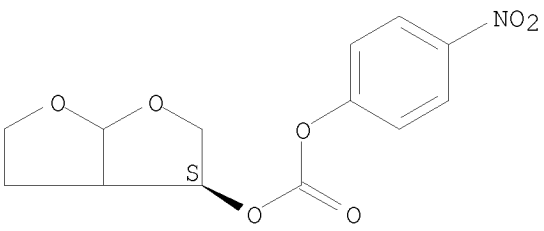
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:699185 HCAPLUS
DOCUMENT NUMBER: 133:267150
TITLE: Preparation of amino acid sulfonamide derivatives as inhibitors of aspartyl protease
INVENTOR(S): Tung, Roger Dennis; Salituro, Francesco Gerald; Deininger, David D.; Murcko, Mark Andrew; Novak, Perry Michael; Bhisetti, Govinda Rao
PATENT ASSIGNEE(S): Vertex Pharmaceuticals, Incorporated, USA
SOURCE: U.S., 74 pp., Cont.-in-part of U.S. Ser. No. 207,580, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6127372	A	20001003	US 1996-424372	19960401
WO 9524385	A1	19950914	WO 1995-US2420	19950224
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1994-207580 B2 19940307
WO 1995-US2420 W 19950224
OTHER SOURCE(S): MARPAT 133:267150
AB Sulfonamides Z-(CH-D)pC(:G)(CXX')mC(:G')N(D')SO2-E' [Z = N(D), SO2E, NH-A, N(D)-A, NH-E, NHC(O)N(D)(E), NH-Ht, N(D)-Ht or phthalimidyl (A = Ht or -R1-Ht, where Ht is a heterocycle which may be substituted, R1 = CO, SO2, COCO, O2C, OSO2, NHSO2, NHCO, NHCOCO, which may be substituted); D, D' = aryl, carbocycle, Ht, alkyl, alkenyl, cycloalkyl, cycloalkenyl, etc.; m = 1-3; p = 0 or 1; G, G' = H2 or O; X, X' = H, OH, NH2, SH, D, halo or XX' = O] were prepared as aspartyl protease inhibitors. Thus, t-BuNHCON(CH2Ph)CH2CH(OH)N(CH2-cyclopentyl)SO2C6H4OMe-p, prepared by sequential reactions of cyclopentylmethylamine, p-methoxybenzenesulfonyl chloride, epibromohydrin, benzylamine, and t-Bu isocyanate, showed Ki = 2,400 for inhibition of HIV-1 protease.
IT 298206-05-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid sulfonamide derivs. as inhibitors of aspartyl protease)
RN 298206-05-0 HCAPLUS
CN Carbonic acid, (3S)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:573770 HCAPLUS
DOCUMENT NUMBER: 133:177157
TITLE: Preparation of [1-benzyl-2-hydroxy-3-(arylsulfonamido)propyl]carbamates as HIV aspartyl protease inhibitors
INVENTOR(S): Hale, Michael R.; Baker, Christopher T.; Stammers, Timothy A.; Sherrill, Ronald G.; Spaltenstein, Andrew; Furfine, Eric S.; Maltais, Francois; Andrews, Clarence Webster, III; Miller, John F.; Samano, Vicente
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 369 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047551	A2	20000817	WO 2000-US3288	20000209
WO 2000047551	A3	20010816		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6319946	B1	20011120	US 2000-500781	20000209
EP 1159278	A2	20011205	EP 2000-913402	20000209
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JP 2002536430	T	20021029	JP 2000-598472	20000209
AT 311391	T	20051215	AT 2000-913402	20000209
EP 1637518	A2	20060322	EP 2005-25977	20000209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
ES 2254156	T3	20060616	ES 2000-913402	20000209
PT 1159278	T	20060630	PT 2000-913402	20000209
TW 260322	B	20060821	TW 2000-89102108	20000209
US 2002198388	A1	20021226	US 2001-927271	20010809

US 6617350	B2	20030909			
US 2004127488	A1	20040701	US 2003-613650		20030702
PRIORITY APPLN. INFO.:			US 1999-120047P	P	19990212
			SY 2000-1090	A	20000207
			EP 2000-913402	A3	20000209
			US 2000-500781	A3	20000209
			WO 2000-US3288	W	20000209
			US 2001-927271	A3	20010809

OTHER SOURCE(S): MARPAT 133:177157

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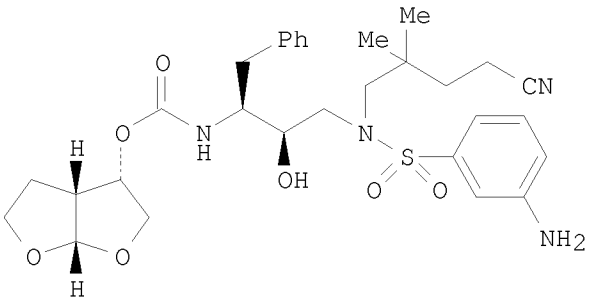


I

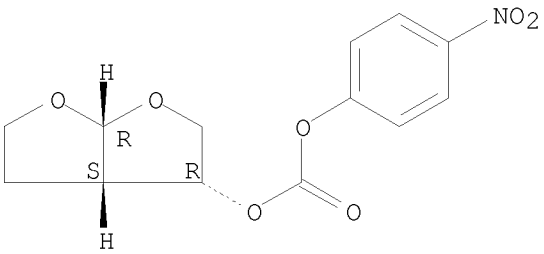
AB ABxN(Gx)CH(D)CH(OR7)CH2ND'E'E [wherein A = H, or (un)substituted Ht, R1Ht, or R1Ak; Ak = alkyl; Ht = cycloalkyl, cycloalkenyl, or (un)substituted aryl or heterocyclyl; R1 = CO(CO), (O)SO2, O2C, or (un)substituted NHSO2 or NHCO(CO); B = (un)substituted NHCH2CO; x = 0 or 1; G = H, R7, alkyl; or G may be bound to R7 to form a heterocyclic ring; R7 = H, (CH2O)xY(ZM)(:X)Z(M)x; etc.; M = H, Li, Na, K, Mg, Ca, Ba, alkyl, alkenyl, etc.; X = O or S; Y = P or S; Z = H, O, S, or (un)substituted NH2; D = independently Q or (un)subsititued (cyclo)alkyl or (cyclo)alkenyl; Q = (un)subsititued carbocylyl or heterocyclyl; D' = (un)substituted alkyl, alkenyl, alkynyl; E = Ht, OHt, HtHt, alkoxy, (un)substituted NH2, alkyl, or carbocyclyl; E' = CO or SO2] were prepared as antiviral agents against HIV-1 and HIV-2 viruses. Thus, 3-NO2C6H4SO2Cl was added to tert-Bu (1S,2R)-N-[1-benzyl-3-[(4-cyano-2,2-dimethylbutyl)amino]-2-hydroxypropyl]carbamate (preparation given) to form the 3-nitrophenylsulfonamide (55%). Reduction to the 3-aminophenylsulfonamide (85%), followed by transesterification with [(3S,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-yl](4-nitrophenyl)carbonate (65%), gave I. In an antiviral activity assay, I inhibited HIV-1 protease in the MT4 cell line with Ki < 1 nM and IC50 < 0.1 μM.

IT 192725-55-6 252873-01-1 252873-35-1
252873-51-1 288296-64-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of heterocyclyl arylsulfonamidopropylcarbamate HIV protease inhibitors by reductive alkylation of amines and subsequent addition of arylsulfonyl chlorides)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 252873-01-1 HCAPLUS
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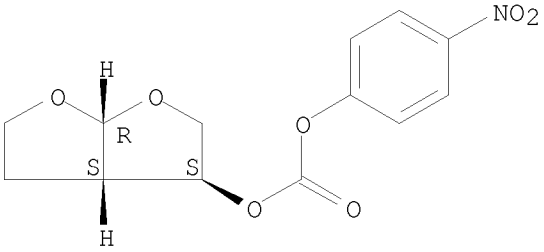
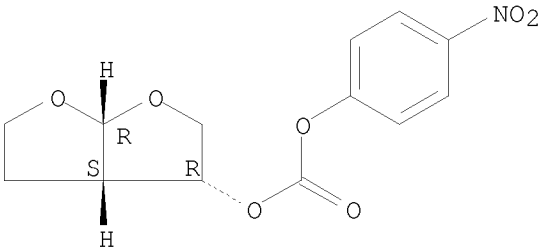
Absolute stereochemistry.



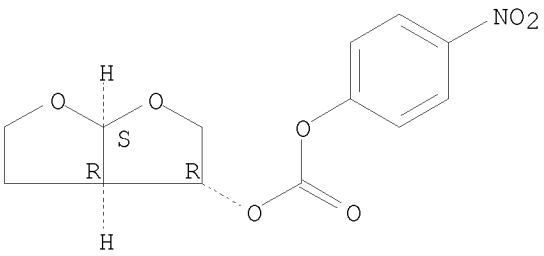
RN 252873-35-1 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester, rel- (CA INDEX NAME)

Relative stereochemistry.



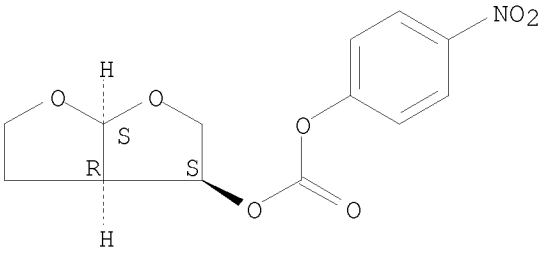
RN 252873-51-1 HCAPLUS
CN Carbonic acid, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



RN 288296-64-0 HCAPLUS
CN Carbonic acid, (3S,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



L15 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:811207 HCAPLUS
DOCUMENT NUMBER: 132:49801
TITLE: Preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compounds as inhibitors of HIV aspartyl protease.
INVENTOR(S): Sherrill, Ronald George; Hale, Michael R.; Spaltenstein, Andrew; Furfine, Eric Steven; Andrews, Clarence Webster, III; Lowen, Gregory Thomas
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 344 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965870	A2	19991223	WO 1999-US13744	19990617
WO 9965870	A3	20010315		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,

	ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	CA 2335477	A1	19991223	CA 1999-2335477		19990617
	AU 9945760	A	20000105	AU 1999-45760		19990617
	AU 767728	B2	20031120			
	EP 1086076	A1	20010328	EP 1999-928769		19990617
	EP 1086076	B1	20041222			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	BR 9912169	A	20010410	BR 1999-12169		19990617
	NZ 508855	A	20031031	NZ 1999-508855		19990617
	AT 285396	T	20050115	AT 1999-928769		19990617
	PT 1086076	T	20050531	PT 1999-928769		19990617
	ES 2235492	T3	20050701	ES 1999-928769		19990617
	AP 1717	A	20070228	AP 2000-2023		19990617
	US 2002049201	A1	20020425	US 2000-731129		20001206
	US 6613743	B2	20030902			
	NO 2000006405	A	20010219	NO 2000-6405		20001215
	MX 2000PA12637	A	20010405	MX 2000-PA12637		20001218
	HK 1037605	A1	20051007	HK 2001-106764		20010925
	US 2004097594	A1	20040520	US 2003-600937		20030620
	NZ 528074	A	20041126	NZ 2003-528074		20030908
	AU 2004200636	A1	20040311	AU 2004-200636		20040219
	US 2006172936	A1	20060803	US 2005-212045		20050825
	AU 2007234578	A1	20071213	AU 2007-234578		20071121
PRIORITY APPLN. INFO.:				US 1998-90094P	P	19980619
				WO 1999-US13744	W	19990617
				US 2000-731129	A3	20001206
				US 2003-600937	B3	20030620
				AU 2004-200636	A3	20040219

OTHER SOURCE(S): MARPAT 132:49801

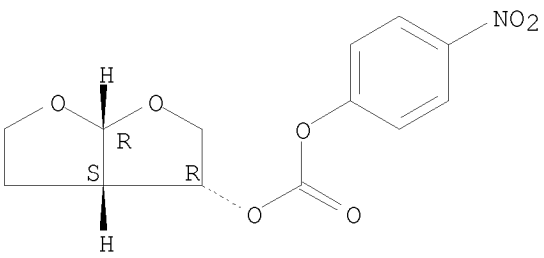
AB ABxN(Gx)CHDCHOR7CH2ND'SO2E [A = H, (substituted) Ht, R1Ht, R1Ak; Ak = alkyl; Ht = cycloalkyl, cycloalkenyl, (substituted) aryl, heterocyclyl; R1 = CO, SO2, COCO, O2C, NR2CO, NR2SO2, etc.; B = null, NR2C(R3)2CO; x = 0, 1; R2 = H, (substituted) Ht, alkyl; R3 = H, (substituted) Ht, alkyl, alkenyl, cycloalkyl, cycloalkenyl; G = null, H, R7, alkyl; G may be bound to R7; D = (substituted) Q, alkyl, alkenyl; Q = (substituted) carbocyclyl, heterocyclyl; D' = OR10, N:R10, N(R10)R1R3; E = Ht, OHt, OR3, NR2R3, (substituted) alkyl, alkenyl, etc.; R7 = H, (CH2O)xY(ZM)(:X)Z(M)x, etc.; M = null, H, Li, Na, K, Mg, Ca, Ba, alkyl, alkenyl, etc.; X = O, S; Y = P, S; Z = O, S, N(R2)2, H], were prepared as inhibitors of HIV aspartyl protease (no data). Thus, 3-H2NC6H4SO2NHOCHMe2 (preparation given), tert-Bu N-(1S)-1-[(2S)-oxiran-2-yl]-2-phenylethylcarbamate, and phosphazene base P4 tert-Bu were stirred in 8 h in THF to give 95% tert-Bu N-(1S,2R)-3-[[(3-aminophenyl)sulfonyl](isopropoxy)amino]-1-benzyl-2-hydroxypropylcarbamate.

IT 192725-55-6 252873-35-1 252873-40-8
252873-51-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compds. as inhibitors of HIV aspartyl protease)

RN 192725-55-6 HCAPLUS

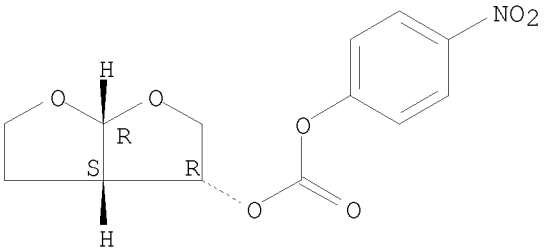
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



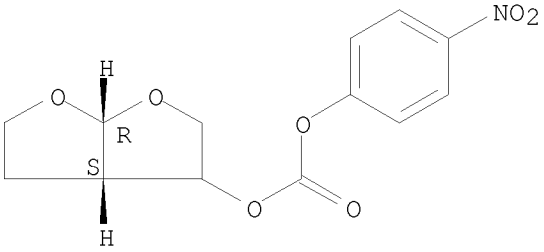
RN 252873-35-1 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester, rel- (CA INDEX NAME)

Relative stereochemistry.



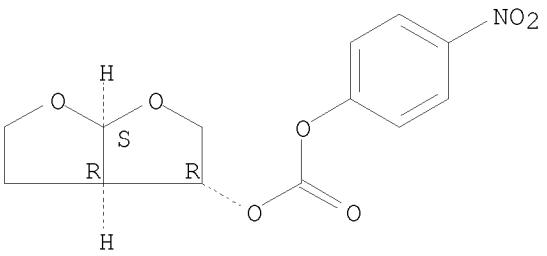
RN 252873-40-8 HCAPLUS
CN Carbonic acid, (3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



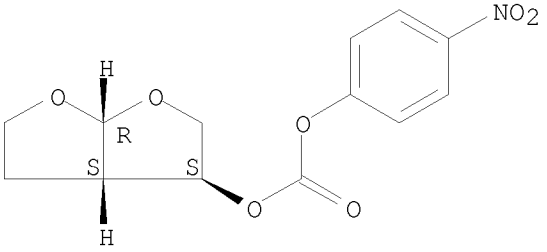
RN 252873-51-1 HCAPLUS
CN Carbonic acid, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



IT 252873-01-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compds. as inhibitors of HIV aspartyl protease)
RN 252873-01-1 HCAPLUS
CN Carbonic acid, (3S,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



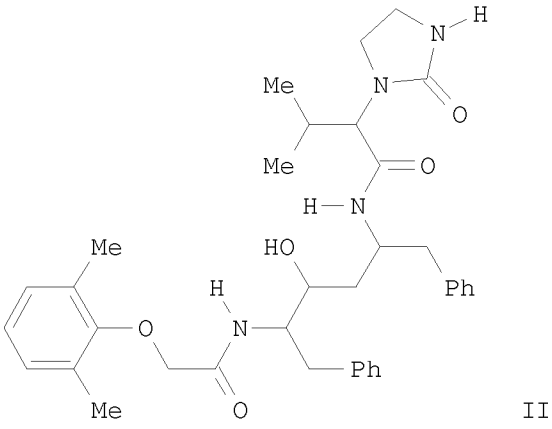
L15 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:393986 HCAPLUS
DOCUMENT NUMBER: 131:59143
TITLE: Preparation of peptide analogs as retroviral protease inhibitors
INVENTOR(S): Sham, Hing Leung; Norbeck, Daniel W.; Chen, Xiaoqi; Betebenner, David A.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 572,226, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5914332	A	19990622	US 1996-753201	19961121
CA 2238978	A1	19970619	CA 1996-2238978	19961206
CA 2238978	C	20010515		

CA 2285119	A1	19970619	CA 1996-2285119	19961206
CA 2285119	C	20050920		
CA 2509505	A1	19970619	CA 1996-2509505	19961206
WO 9721685	A1	19970619	WO 1996-US20440	19961206
W: AU, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9713422	A	19970703	AU 1997-13422	19961206
AU 725369	B2	20001012		
EP 882024	A1	19981209	EP 1996-944941	19961206
EP 882024	B1	20020206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1208405	A	19990217	CN 1996-199904	19961206
HU 9901079	A2	19990928	HU 1999-1079	19961206
HU 223782	B1	20050128		
JP 2000502085	T	20000222	JP 1997-522278	19961206
JP 3170292	B2	20010528		
HU 20003305	A3	20001228	HU 2000-3305	19961206
HU 222731	B1	20030929		
JP 2001058979	A	20010306	JP 2000-190510	19961206
EP 1170289	A2	20020109	EP 2001-124290	19961206
EP 1170289	A3	20021113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AT 212986	T	20020215	AT 1996-944941	19961206
PT 882024	T	20020731	PT 1996-944941	19961206
ES 2173341	T3	20021016	ES 1996-944941	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
NZ 510329	A	20040227	NZ 1996-510329	19961206
CZ 293650	B6	20040616	CZ 2000-2210	19961206
CZ 294246	B6	20041110	CZ 1998-1762	19961206
NZ 510328	A	20050128	NZ 1996-510328	19961206
IL 156237	A	20050517	IL 1996-156237	19961206
NZ 338003	A	20050826	NZ 1996-338003	19961206
CZ 296915	B6	20060712	CZ 2004-762	19961206
ZA 9610475	A	19970731	ZA 1996-10475	19961212
TW 494097	B	20020711	TW 1997-86101654	19970213
TW 259178	B	20060801	TW 2000-89115157	19970213
US 6284767	B1	20010904	US 1998-207873	19981208
HK 1016585	A1	20020809	HK 1999-101462	19990409
US 6313296	B1	20011106	US 2000-511390	20000223
US 2002004503	A1	20020110	US 2001-837280	20010418
US 6472529	B2	20021029		
US 2003100755	A1	20030529	US 2002-280652	20021025
US 7279582	B2	20071009		

PRIORITY APPLN. INFO.:	US 1995-572226	B2 19951213
	US 1996-753201	A 19961121
	US 1996-754687	A 19961121
	CA 1996-2238978	A3 19961206
	CA 1996-2285119	A3 19961206
	EP 1996-943605	A3 19961206
	EP 1996-944941	A3 19961206
	IL 1996-124607	A3 19961206
	JP 1997-522278	A3 19961206
	WO 1996-US20440	W 19961206
	US 1998-207873	A3 19981208
	US 2001-837280	A3 20010418

OTHER SOURCE(S): MARPAT 131:59143
GI



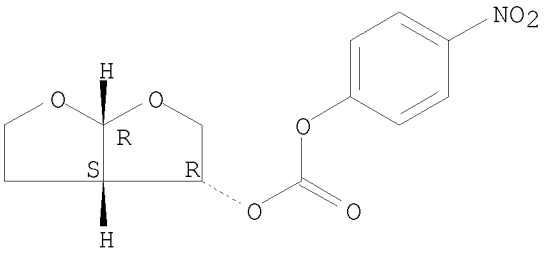
II

AB R4Z1CONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [I; R1,R2 = lower alkyl, cycloalkylalkyl, arylalkyl; R3 = lower alkyl, hydroxyalkyl, cycloalkylalkyl; R4 = aryl, heterocyclyl; R5 = N-attached (thi)oxo- or iminoazacycloalkyl; Z1 = Z, O, S, (alkyl)imino, OZ, ZO, NHZ, etc.; Z = alkylene] were prepared Thus, title compound (S,S,S)-II was prepared in 8 steps
from L-phenylalanine. Data for biol. activity of I were given.

IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:515728 HCAPLUS
DOCUMENT NUMBER: 127:122001

TITLE: Preparation of peptide analogs as retroviral protease inhibitors

INVENTOR(S): Sham, Hing Leung; Norbeck, Daniel W.; Chen, Xiaoqi; Betebenner, David A.; Kempf, Dale J.; Herrin, Thomas R.; Kumar, Gondi N.; Condon, Stephen L.; Cooper, Arthur J.; Dickman, Daniel A.; Hannick, Steven M.; Kolaczkowski, Lawrence; Oliver, Patricia A.; Plata, Daniel J.; Stengel, Peter J.; Stoner, Eric J.; Tien, Jieh-Heh J.; Liu, Jih-Hua; Patel, Ketan M.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721685	A1	19970619	WO 1996-US20440	19961206
W: AU, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5914332	A	19990622	US 1996-753201	19961121
AU 9713422	A	19970703	AU 1997-13422	19961206
AU 725369	B2	20001012		
EP 882024	A1	19981209	EP 1996-944941	19961206
EP 882024	B1	20020206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
HU 9901079	A2	19990928	HU 1999-1079	19961206
HU 223782	B1	20050128		
JP 2000502085	T	20000222	JP 1997-522278	19961206
JP 3170292	B2	20010528		
HU 20003305	A3	20001228	HU 2000-3305	19961206
HU 222731	B1	20030929		
AT 212986	T	20020215	AT 1996-944941	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
IL 156237	A	20050517	IL 1996-156237	19961206
HK 1016585	A1	20020809	HK 1999-101462	19990409

PRIORITY APPLN. INFO.:	US 1995-572226	A	19951213
	US 1996-753201	A	19961121
	US 1996-754687	A	19961121
	EP 1996-943605	A3	19961206
	IL 1996-124607	A3	19961206
	WO 1996-US20440	W	19961206

OTHER SOURCE(S): MARPAT 127:122001

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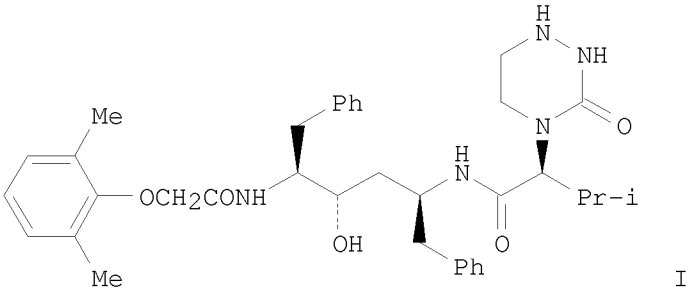


I

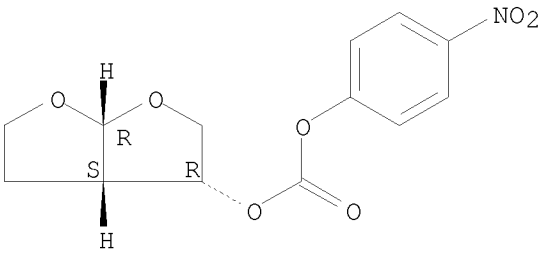
AB R4 -L1-CONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [R1, R2 = lower alkyl, cycloalkylalkyl, arylalkyl; R3 = lower alkyl, hydroxyalkyl, cycloalkylalkyl; R4 = aryl, heterocyclyl; R5 = heterocyclyl e.g. Q - Q4; wherein m, n = 1-3; p = 1,2; X = O, S, NH; Y = CH2, O, S, (un)substituted NH; Z = O, S, NH; L1 = O, S, (un)substituted NH, O-alkylenyl, S(O)m-alkylenyl (wherein m = 0, 1,2), N-(un)substituted NH-alkylenyl, alkylenyl, alkenylenyl, etc.] are prepared Methods and compns. for inhibiting an HIV infection are also disclosed. Thus, (2S)-(4-benzyloxycarbonylaza-1-tetrahydropyrimid-2-onyl)-3-methylbutanoic acid (preparation given) was condensed with (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-amino-1,6-diphenylhexane using standard coupling procedure [1-ethyl-3-(3-dimethylaminopropyl)carbodiimide/DMF] followed by hydrogenolysis over 10% Pd-C to give the title compound (I). I in vitro at 0.5 nmol inhibited HIV protease by 94.6%.

IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:515727 HCAPLUS
DOCUMENT NUMBER: 127:121994
TITLE: Preparation and formulation of N-(α-aminoacyl)diaminohydroxyalkanes as HIV protease inhibitors

INVENTOR(S): Sham, Hing Leung; Stewart, Kent D.; Kempf, Dale J.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721683	A1	19970619	WO 1996-US19394	19961206
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2238977	A1	19970619	CA 1996-2238977	19961206
EP 876353	A1	19981111	EP 1996-943605	19961206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000502997	T	20000314	JP 1997-522112	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.:

US 1995-572226	A	19951213
US 1996-754687	A	19961121
EP 1996-943605	A3	19961206
WO 1996-US19394	W	19961206

OTHER SOURCE(S): MARPAT 127:121994
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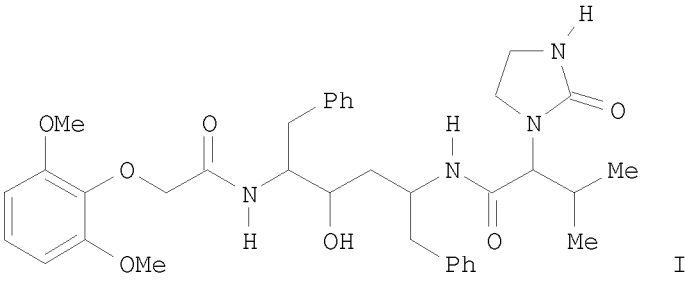


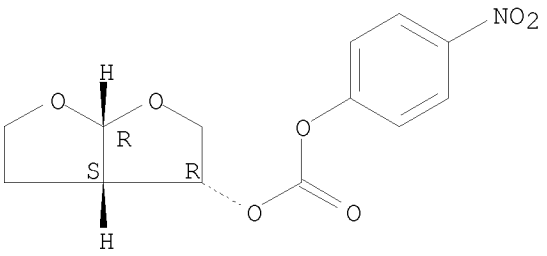
I

AB R4ZCONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [I; R1,R2 = (cyclo)alkyl, aralkyl; R3 = (cyclo)alkyl, hydroxyalkyl; R4 = heterocyclyl or aryl; R5 = N-attached oxoheterocyclyl, etc.] were prepared Thus, (S)-(PhCH2)2NCH(CH2Ph)COCH2CN (preparation given) was condensed with PhCH2MgCl and the product reduced by NaBH4 to give (S,S,S)-(PhCH2)2NCH(CH2Ph)CH(OH)CH2CH(NH2)CH2Ph. The latter was N-protected and the N-debenzylated product amidated by 2,6-(MeO)C6H3OCH2CO2H (preparation given) to give, after deprotection and amidation by (S)-Me2CHCHR5CO2H (R5 = 2-oxo-1H-imidazol-3-yl)(preparation given), title compound (S,S,S,S)-II. Data for biol. activity of I were given.

IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and formulation of N-(α-aminoacyl)diaminohydroxyalkanes as HIV protease inhibitors)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> d ibib abs hitstr 1-34 l14

L14 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1207559 HCAPLUS
DOCUMENT NUMBER: 147:502107
TITLE: Preparation of 2-({4-chloro-2-[(3-chloro-5-cyanophenyl)carbonyl]phenyl}oxy)-N-(4-{[(2S)-2,3-dihydroxy-3-methylbutyl}oxy}-2-methylphenyl}acetamide as a non-nucleoside reverse transcriptase inhibitor
INVENTOR(S): Aquino, Christopher Joseph; Freeman, George Andrew; Martin, Michael Tolar
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 34pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007121415	A2	20071025	WO 2007-US66733	20070417
WO 2007121415	A3	20071221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2006-792496P P 20060417

US 2006-863846P P 20061101

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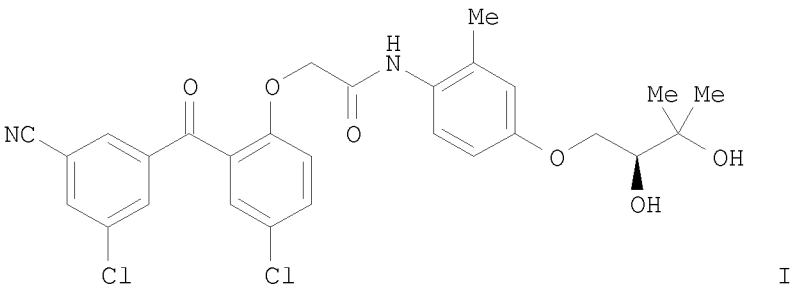


I

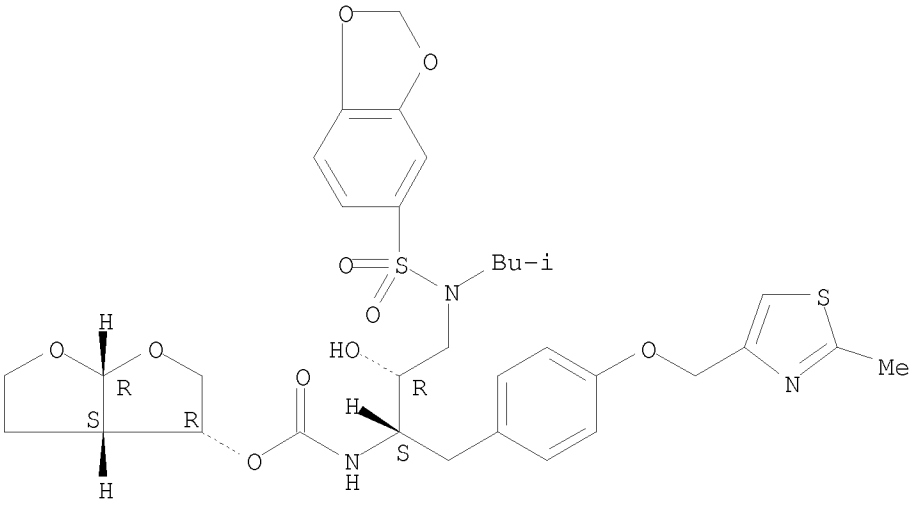
AB The present invention relates to a compound I that is a non-nucleoside reverse transcriptase inhibitor, and to processes for the preparation and use of the same. I was prepared in a multi-step synthesis, starting from (2S)-2,3-dihydroxy-3-methylbutyl 4-methylbenzenesulfonate. Specifically, the present invention includes methods of using compound I in the treatment of human immunodeficiency virus infection. I was tested against wild type and clin. relevant HIV (IC50 data were given). Pharmaceutical composition comprising the compound I alone and in combination with other therapeutic agents are disclosed.

IT 313682-08-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 2-(phenylcarbonylphenoxy)-N-(dihydroxymethylbutoxyphenyl)acetamide as non-nucleoside reverse transcriptase inhibitors useful in combination therapy of HIV infection)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.

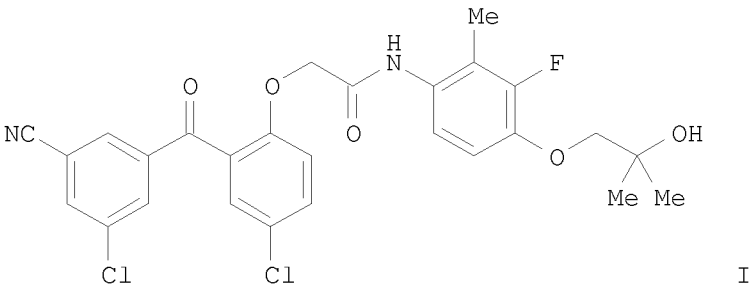


L14 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1207558 HCAPLUS
DOCUMENT NUMBER: 147:502106
TITLE: Preparation of 2-({4-chloro-2-[(3-chloro-5-cyanophenyl)carbonyl]phenyl}oxy)-N-{3-fluoro-4-[(2-hydroxy-2-methylpropyl)oxy]-2-methylphenyl}acetamide as a non-nucleoside reverse transcriptase inhibitor
INVENTOR(S): Aquino, Christopher Joseph; Freeman, George Andrew; Martin, Michael Tolar
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 27pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007121418	A2	20071025	WO 2007-US66736	20070417
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2006-792543P P 20060417
US 2006-863846P P 20061101

GI



I

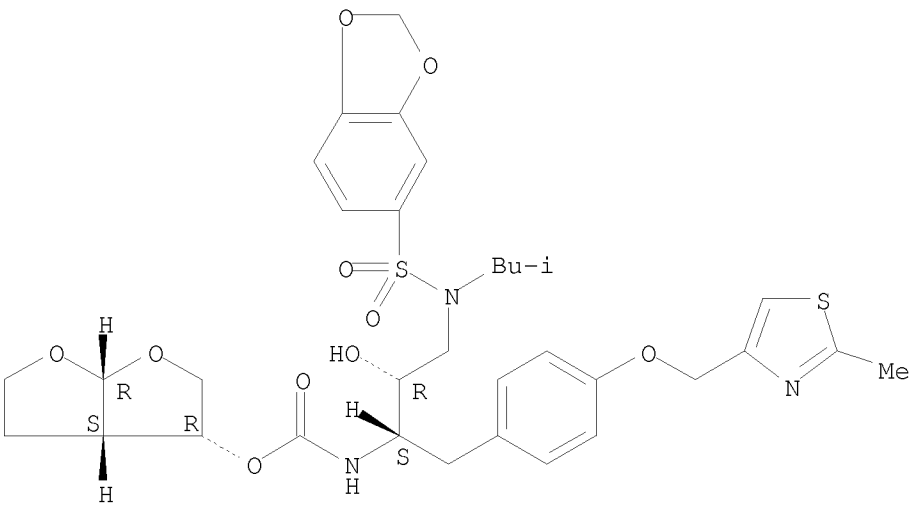
AB The present invention relates to a compound I that is a non-nucleoside reverse transcriptase inhibitor, and to processes for the preparation and use of the same. I was prepared in a multi-step synthesis, starting from (2,3-difluoro-6-nitrophenyl)acetic acid. Specifically, the present invention includes methods of using compound I in the treatment of human immunodeficiency virus infection. I was tested against wild type and clin. relevant HIV (IC50 data were given). Pharmaceutical composition comprising the compound I alone and in combination with other therapeutic agents are disclosed.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 2-(phenylcarbonylphenoxy)-N-(hydroxypropoxyphenyl)acetamide as non-nucleoside reverse transcriptase inhibitors useful in combination therapy of HIV infection)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



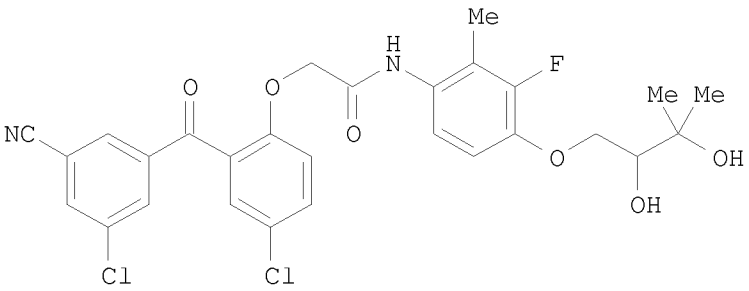
L14 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1207557 HCAPLUS
DOCUMENT NUMBER: 147:502105
TITLE: Preparation of 2-({4-chloro-2-[(3-chloro-5-cyanophenyl)carbonyl]phenyl}oxy)-N-{4-[(2,3-dihydroxy-3-methylbutyl)oxy]-3-fluoro-2-methylphenyl}acetamide as a non-nucleoside reverse transcriptase inhibitor
INVENTOR(S): Aquino, Christopher Joseph; Freeman, George Andrew; Martin, Michael Tolar
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 36pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007121416	A2	20071025	WO 2007-US66734	20070417

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-792434P P 20060417
US 2006-863846P P 20061101

GI



I

AB The present invention relates to a compound I that is a non-nucleoside reverse transcriptase inhibitor, and to processes for the preparation and use of the same. Compds. (2S)-I, (2R)-I and rac-I were prepared For example, I was prepared in a multi-step synthesis, starting from (2,3-difluoro-6-nitrophenyl)acetic acid. Specifically, the present invention includes

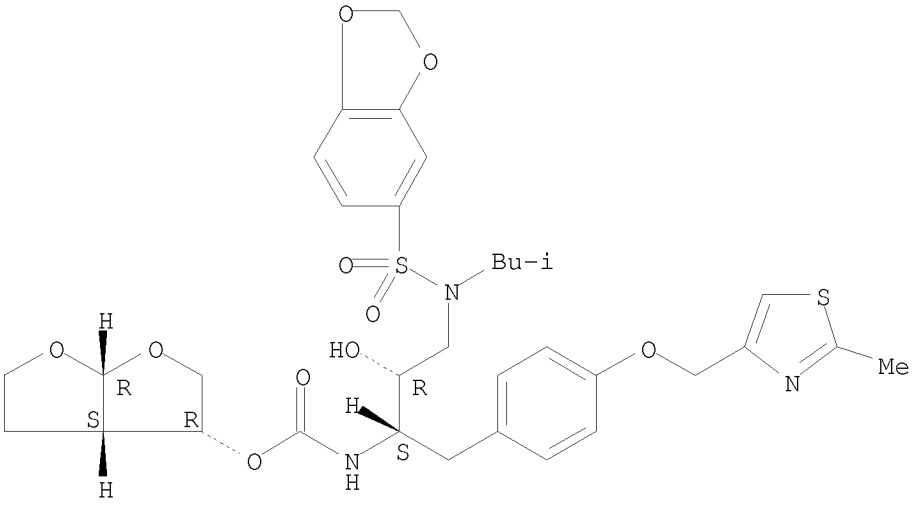
methods of using compound I in the treatment of human immunodeficiency virus infection. (2S)-I, (2R)-I and rac-I were tested against wild type and clin. relevant HIV (IC50 data were given). Pharmaceutical composition comprising the compound I alone and in combination with other therapeutic agents are disclosed.

IT 313682-08-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 2-(phenylcarbonylphenoxy)-N-(hydroxymethylbutoxyphenyl)acetamide as non-nucleoside reverse transcriptase inhibitor useful in combination therapy of HIV infection)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1075740 HCAPLUS

DOCUMENT NUMBER: 147:495981

TITLE: Potent Inhibition of HIV-1 Replication by Novel Non-peptidyl Small Molecule Inhibitors of Protease Dimerization

AUTHOR(S): Koh, Yasuhiro; Matsumi, Shintaro; Das, Debananda; Amano, Masayuki; Davis, David A.; Li, Jianfeng; Leschenko, Sofiya; Baldridge, Abigail; Shioda, Tatsuo; Yarchoan, Robert; Ghosh, Arun K.; Mitsuya, Hiroaki

CORPORATE SOURCE: Department of Hematology, Kumamoto University Graduate School of Medical and Pharmaceutical Sciences, Honjo, 860-8556, Japan

SOURCE: Journal of Biological Chemistry (2007), 282(39), 28709-28720
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular

Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

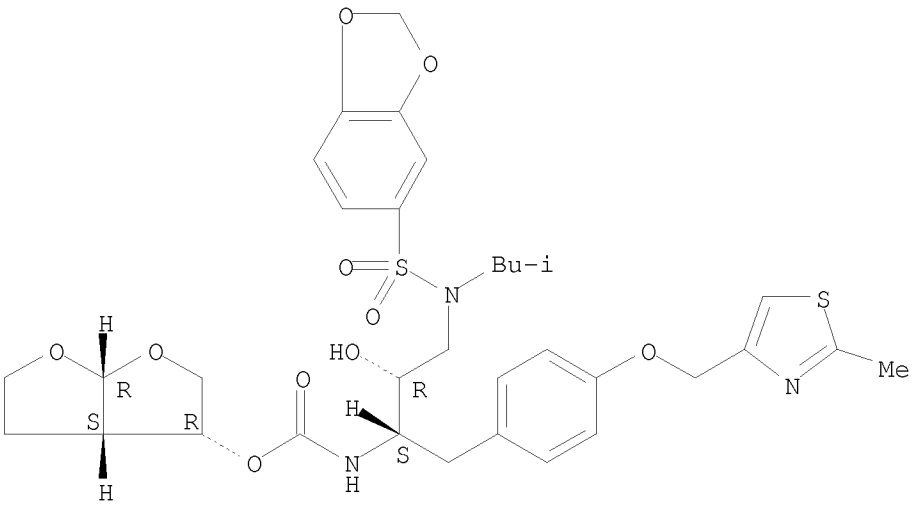
AB Dimerization of HIV-1 protease subunits is essential for its proteolytic activity, which plays a critical role in HIV-1 replication. Hence, the inhibition of protease dimerization represents a unique target for potential intervention of HIV-1. The authors developed an intermol. fluorescence resonance energy transfer-based HIV-1-expression assay employing cyan and yellow fluorescent protein-tagged protease monomers. Using this assay, the authors identified nonpeptidyl small mol. inhibitors of protease dimerization. These inhibitors, including darunavir and two exptl. protease inhibitors, blocked protease dimerization at concns. of as low as 0.01 μM and blocked HIV-1 replication with IC50 values of 0.0002-0.48 μM. These agents also inhibited the proteolytic activity of mature protease. Other approved anti-HIV-1 agents examined except tipranavir, a CCR5 inhibitor, and soluble CD4 failed to block the dimerization event. Once protease monomers dimerize to become mature protease, mature protease is not dissociated by this dimerization inhibition mechanism, suggesting that these agents block dimerization at the nascent stage of protease maturation. The proteolytic activity of mature protease that managed to undergo dimerization despite the presence of these agents is likely to be inhibited by the same agents acting as conventional protease inhibitors. Such a dual inhibition mechanism should lead to highly potent inhibition of HIV-1.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potent inhibition of HIV-1 replication by novel non-peptidyl small mol. inhibitors of protease dimerization)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.

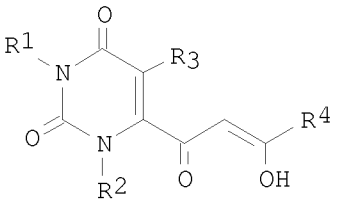


REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1064150 HCAPLUS
DOCUMENT NUMBER: 147:385768
TITLE: Diketo acids with nucleobase scaffolds: anti-HIV replication inhibitors targeted at HIV integrase in combination therapy
INVENTOR(S): Nair, Vasu; Chi, Guochen; Uchil, Vinod R.
PATENT ASSIGNEE(S): University of Georgia Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 110pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007106450	A2	20070920	WO 2007-US6245	20070309
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2006-781520P P 20060310
OTHER SOURCE(S): CASREACT 147:385768; MARPAT 147:385768
GI



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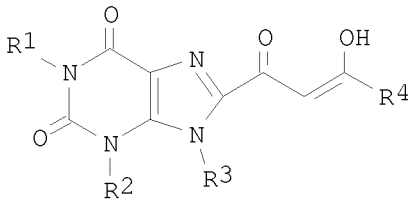
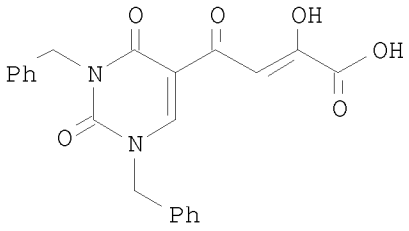


II



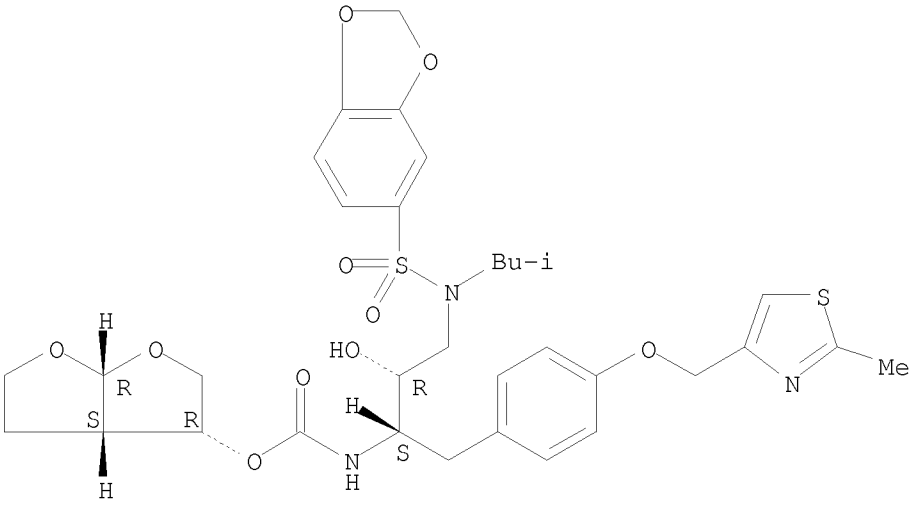
III

AB A new class of diketo acids constructed on nucleobase scaffolds, e.g., I [R1, R2 = (un)substituted CH2Ph whereby Ph is substituted with 1 to 3 substituents selected from halogen, OH, OMe, Me, Et, Pr, CF3, CH2Rb; Rb = 5- or 6-membered heteroarom.; R3 = H, C1-6-alkyl, halogen, (un)susbtituted CH2Ph, (un)substituted SPh, whereby Ph is substituted with 1 to 3 substituents selected from halogen, OH, OMe, Me, Et, Pr, CF3; R4 = CO2R; R = H, C1-6-alkyl] and II, designed as inhibitors of HIV replication through inhibition of HIV integrase, is described. Thus, 4-(1,3-dibenzyl-1,2,3,4-tetrahydro-2,4-dioxopyrimidin-5-yl)-2-hydroxy-4-oxo-2-butenoic acid (III) was prepd from 5-acetyluracil via dibenzylation with PhCH2Br in DMF containing K2CO3, condensation with MeO2CCO2Me in THF containing NaOCMe3, and acid hydrolysis with aqueous HCl in dioxane. These compds. are useful in the prevention or treatment of infection by HFV and in the treatment of AIDS and ARC, either as the compds., or as pharmaceutically acceptable salts, with pharmaceutically acceptable carriers, in combination with antivirals, immunomodulators, antibiotics, vaccines, and other therapeutic agents, especially other anti-HIV compds. (including other anti-HIV integrase agents), which can be used to create combination anti- HIV cocktails as disclosed herein. Methods of treating AIDS and ARC and methods of treating or preventing infection by HIV are also described. Compds. of the present application include those of I and include tautomers, regioisomers, geometric isomers, and where applicable, optical isomers thereof, and pharmaceutically acceptable salts thereof, wherein the nucleobase scaffold and R groups are as otherwise defined in the specification. These are combined with any number of typical other anti-HIV agents to provide an effective treatment modality for HIV infections, including AIDS and ARC. The bioactivity of III was determined [IC50 = 0.02 μM; CC50 = >2000 μM; Therapeutic Index = >10,000 vs. HIV integrase in vitro].

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel diketo acids constructed on nucleobase scaffolds as inhibitors

of HIV replication through inhibition of HIV integrase useful in prevention and combination therapy of infections)
RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1021139 HCAPLUS
DOCUMENT NUMBER: 147:335724
TITLE: In vitro antiviral activity of the novel, tyrosyl-based human immunodeficiency virus (HIV) type 1 protease inhibitor brecanavir (GW640385) in combination with other antiretrovirals and against a panel of protease inhibitor-resistant HIV
AUTHOR(S): Hazen, Richard; Harvey, Robert; Ferris, Robert; Craig, Charles; Yates, Phillip; Griffin, Philip; Miller, John; Kaldor, Istvan; Ray, John; Samano, Vincente; Furfine, Eric; Spaltenstein, Andrew; Hale, Michael; Tung, Roger; St. Clair, Marty; Hanlon, Mary; Boone, Lawrence
CORPORATE SOURCE: Metabolic and Viral Diseases CEDD, Department of Virology, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(9), 3147-3154
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Brecanavir, a novel tyrosyl-based arylsulfonamide, high-affinity, human immunodeficiency virus type 1 (HIV-1) protease inhibitor (PI), has been evaluated for anti-HIV activity in several in vitro assays. Preclin.

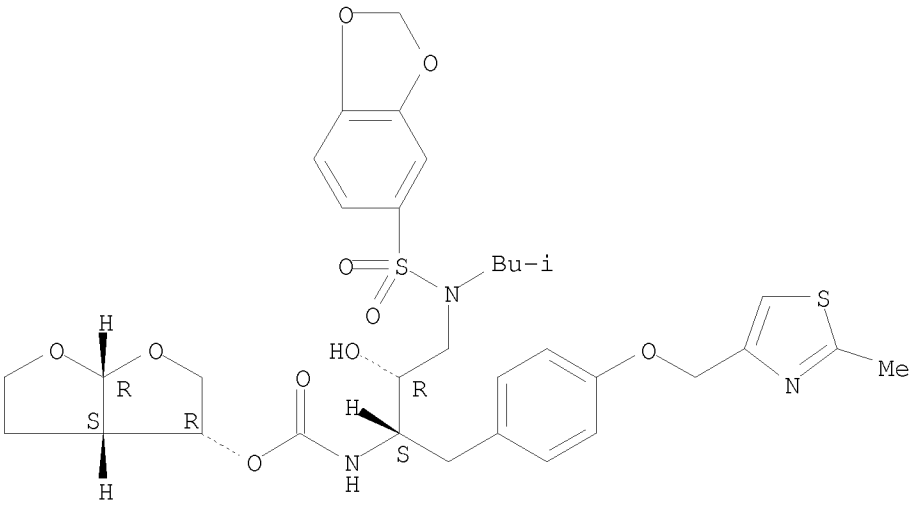
assessment of brecanavir indicated that this compound potently inhibited HIV-1 in cell culture assays with 50% effective concns. (EC50s) of 0.2 to 0.53 nM and was equally active against HIV strains utilizing either the CXCR4 or CCR5 coreceptor, as was found with other PIs. The presence of up to 40% human serum decreased the anti-HIV-1 activity of brecanavir by 5.2-fold, but under these conditions the compound retained single-digit nanomolar EC50s. When brecanavir was tested in combination with nucleoside reverse transcriptase inhibitors, the antiviral activity of brecanavir was synergistic with the effects of stavudine and additive to the effects of zidovudine, tenofovir, dideoxycytidine, didanosine, adefovir, abacavir, lamivudine, and emtricitabine. Brecanavir was synergistic with the nonnucleoside reverse transcriptase inhibitor nevirapine or delavirdine and was additive to the effects of efavirenz. In combination with other PIs, brecanavir was additive to the activities of indinavir, lopinavir, nelfinavir, ritonavir, amprenavir, saquinavir, and atazanavir. Clin. HIV isolates from PI-experienced patients were evaluated for sensitivity to brecanavir and other PIs in a recombinant virus assay. Brecanavir had a <5-fold increase in EC50s against 80% of patient isolates tested and had a greater mean in vitro potency than amprenavir, indinavir, lopinavir, atazanavir, tipranavir, and darunavir. Brecanavir is by a substantial margin the most potent and broadly active antiviral agent among the PIs tested in vitro.

IT 313682-08-5, GW 640385
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro antiviral activity of tyrosyl-based HIV-1 protease inhibitor brecanavir (GW640385) in combination with other antiretrovirals and against panel of protease inhibitor-resistant HIV)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS

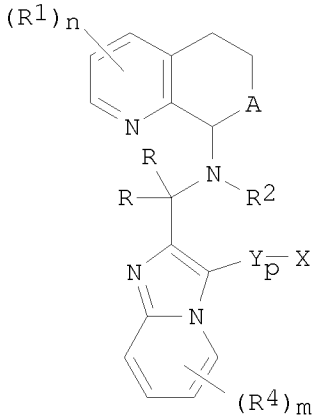
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:845883 HCAPLUS
DOCUMENT NUMBER: 147:235169
TITLE: Imidazo[1,2-a]pyridine-3-carboxamides as anti-HIV agents and their preparation, pharmaceutical compositions and their use in monotherapy and in combination therapy of diseases
INVENTOR(S): Gudmundsson, Kristjan; Turner, Elizabeth Madalena
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Svolto, Angilique Christina
SOURCE: PCT Int. Appl., 104pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

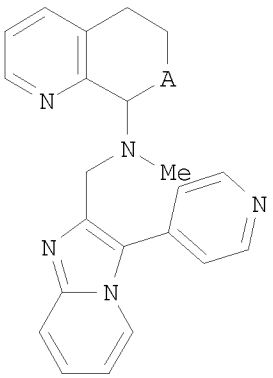
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007087548	A2	20070802	WO 2007-US60938	20070124
WO 2007087548	A9	20070927		
WO 2007087548	A3	20071213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2006-761883P P 20060125
OTHER SOURCE(S): MARPAT 147:235169
GI



I



II

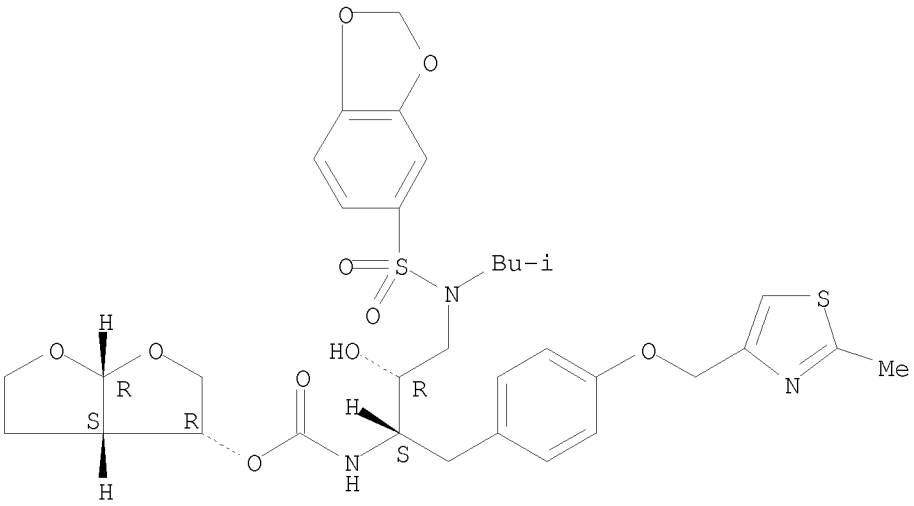
AB The invention provides compds. of formula I including salts, solvates, and pharmaceutically acceptable derivs. thereof, pharmaceutical formulations containing them, processes for their preparation, and methods of treatment using them. Compds. of formula I wherein A is (CH2)0-2; each R is independently H, C1-8 (halo)alkyl, C2-8 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, etc.; ech R1 is independently halo, C1-8 (halo)alkyl, C2-8 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, C3-8 cycloalkenyl, etc.; n and m are independently 0, 1 and 2; R2 is H, C1-8 (halo)alkyl, C3-8 cycloalkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; p is 0 and 1; Y is NH and derivs., O, CONH and derivs., NHCO and derivs., CO, CO2, NHCONH and derivs., S, SO, SO2, etc.; X is (un)substituted (hetero)arylamine, (un)substituted (hetero)aryl, (un)substituted heterocyclyl, etc.; R4 is halo, C1-8 (halo)alkyl, C2-6 alkenyl, C2-6 alkynyl, C2-8 cycloalkyl, OH and derivs., CN, NO2, etc.; and their pharmaceutically acceptable derivs. thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their anti-HIV activity. From the assay, it was determined that the tested compds. exhibited IC50 values of about 1 nM to about 50 μM.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of imidazopyridinecarboxamides as anti-HIV agents useful in monotherapy and in combination therapy of diseases)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

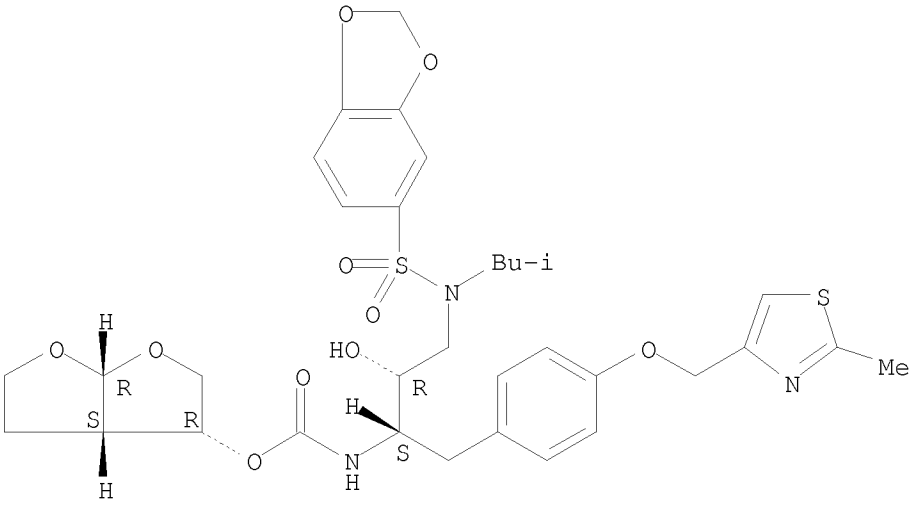
Absolute stereochemistry.



L14 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:823853 HCAPLUS

DOCUMENT NUMBER: 147:132968
TITLE: Preliminary safety and efficacy data of brecanavir, a novel HIV-1 protease inhibitor: 24 week data from study HPR10006
AUTHOR(S): Lalezari, Jacob P.; Ward, Douglas J.; Tomkins, Susan A.; Garges, Harmony P.
CORPORATE SOURCE: Quest Clinical Research, Department of Medicine, University of California at San Francisco, San Francisco, CA, USA
SOURCE: Journal of Antimicrobial Chemotherapy (2007), 60(1), 170-174
CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Brecanavir, a novel protease inhibitor (PI), has sub-nM in vitro antiviral activity against multi-PI-resistant HIV-1 and in vitro is >100-fold more potent than previously marketed PIs and approx. 10-fold more potent than the recently marketed PI, darunavir. HPR10006 is an open label, single-arm, descriptive 48 wk study, with 8 and 24 wk interim analyses. Thirty-one HIV-1-infected patients were enrolled and received brecanavir/ritonavir 300 mg/100 mg twice daily, with two nucleoside reverse transcriptase inhibitors, based on history and genotype. At baseline, 25/31 had PI-sensitive virus and 6/31 had PI-resistant virus (median of two primary PI and five secondary PI mutations). Median baseline HIV-1 RNA was 5.0 and 4.2 log10 copies/mL, resp. Four patients discontinued prior to Week 24. At Week 24, 77% (24/31) had HIV-1 RNA <50 copies/mL regardless of screening genotype, including 5/6 patients with PI-resistant virus (6/6 had HIV-1 RNA <400 copies/mL). Brecanavir/ritonavir was well tolerated with no serious adverse events or clin. concerning changes in laboratory parameters. Of 31 patients, 10 (32%) experienced drug-related Grade 2-4 adverse events [most frequent events were fatigue (13%), dyspepsia (10%) and nausea (10%)]. Baseline isolate brecanavir IC50 values for all patients ranged from 0.1 to 0.2 nM. Median plasma trough concentration at Week 4 was 150 ng/mL. Correcting the IC50 (0.2 nM) value for protein binding (6-fold increase in vitro with 50% human serum) gives a corrected inhibitory quotient of 180. Brecanavir/ritonavir was well tolerated and showed potent antiviral activity in HIV-1-infected patients harbouring both PI-sensitive and PI-resistant virus, following 24 wk of dosing.
IT 313682-08-5, Brecanavir
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV-1 protease inhibitor brecanavir safety and efficacy)
RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



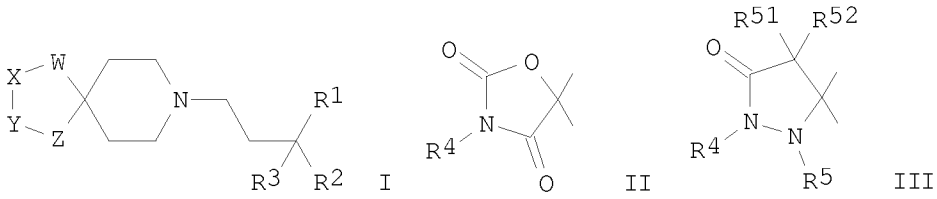
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

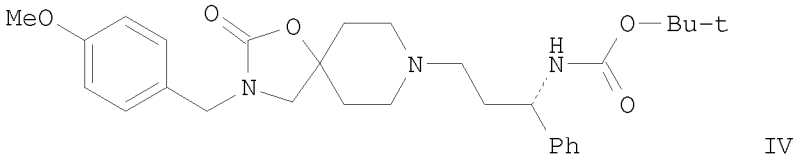
L14 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:642553 HCAPLUS
DOCUMENT NUMBER: 147:72745
TITLE: Preparation of novel spiropiperidine compounds for the modulation of chemokine receptor activity
INVENTOR(S): Moinet, Christophe; Courchesne, Marc
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 81pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007065256	A1	20070614	WO 2006-CA1981	20061205

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-742545P P 20051206
OTHER SOURCE(S): MARPAT 147:72745
GI





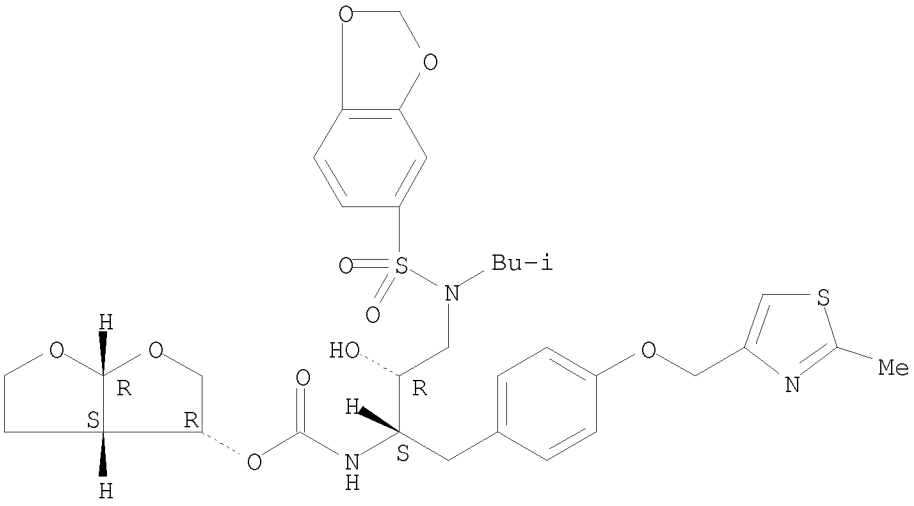
AB The title compds. I [ring containing W, X, Y and Z = II, III, etc.; R1 = NR6C(O)R7, NR6C(O)OR7, etc.; R2 = alkyl, alkenyl, aryl, etc.; R3 = H, alkyl, aryl; R4, R5, R51, R52 = H, alkyl, aryl, etc.; R6 = H, alkyl, alkenyl, alkynyl; R7 = H, alkyl, alkenyl, aryl, etc.], useful for the modulation of CCR5 chemokine receptor activity, particularly in the prevention or treatment of inflammatory diseases, immunoregulatory diseases, organ transplantation reactions and infectious diseases such as HIV infections, were prepared and claimed. E.g., a multi-step synthesis of (S)-IV, starting from tert-Bu 2-oxo-1-oxa-3,8-diaza-spiro[4.5]decane-8-carboxylate and 4-methoxybenzyl chloride, was given. Compds. I have been found to have activity in binding to the CCR5 receptor, generally with an IC50 value of less than 25 μM. Certain compds. I have also been tested in an assay for HIV activity and generally having an IC50 value of less than 1 μM.

IT 313682-08-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of novel spiropiperidine compds. as chemokine receptor modulators useful in treatment and prevention of diseases)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:437040 HCAPLUS
DOCUMENT NUMBER: 146:394423
TITLE: Safety and pharmacokinetics of brecanavir, a novel human immunodeficiency virus type 1 protease inhibitor, following repeat administration with and without ritonavir in healthy adult subjects
AUTHOR(S): Reddy, Y. Sunila; Ford, Susan L.; Anderson, Maggie T.; Murray, Sharon C.; Ng-Cashin, Judith; Johnson, Mark A.
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(4), 1202-1208
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Brecanavir (BCV) is a novel, potent protease inhibitor in development for the treatment of human immunodeficiency virus (HIV-1) infection with low nM in vitro 50% inhibitory concns. (IC50s) against many multiprotease inhibitor resistant viruses. This study was a double-blind, randomized, placebo-controlled repeat-dose escalation to evaluate the safety, tolerability, and pharmacokinetics of BCV, with or without ritonavir (RTV), in 68 healthy subjects. Seven sequential cohorts (n = 10) received BCV (50 to 600 mg) in combination with 100 mg RTV (every 12 h [q12h] or q24h) or alone at 800 mg q12h for 15 days. BCV alone or in combination with RTV was well tolerated, with no serious adverse events reported. The most common drug-related adverse event was headache. BCV was readily absorbed with median time to maximum concentration of drug in serum values ranging from 2.5 to 5.0 h postdose following single- and repeat-dose administration of BCV alone and BCV with RTV 100 mg. Geometric mean BCV accumulation ratios ranged from 1.4 to 1.56 following BCV-RTV q24h regimens and from 1.84 to 4.93 following BCV q12h regimens. BCV steady

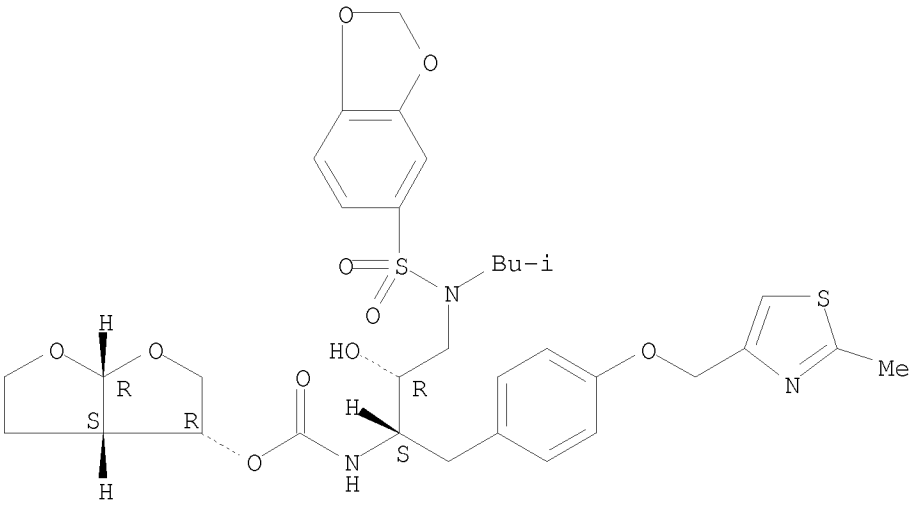
state was generally achieved by day 13 in all groups. All day 15 BCV-RTV trough concentration values in q12h regimens reached or surpassed the estimated protein-binding corrected in vitro IC50 target BCV concentration of 28 ng/mL for highly resistant isolates. The pharmacokinetic and safety profile of BCV-RTV supports continued investigation in HIV-1-infected subjects.

IT 313682-08-5, Brecanavir
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV-1 antiviral brecanavir safety and pharmacokinetics: repeat administration with and without ritonavir in healthy humans)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:351992 HCAPLUS
DOCUMENT NUMBER: 146:379833
TITLE: Preparation of pyridinylaminosulfonylarylcarboxamides as cytochrome P450 3A4 inhibitors
INVENTOR(S): Patterson, Brian Douglas; Sakata, Sylvie Kim; Nambu, Mitchell David; Patel, Leena Bharat Kumar; Tatlock, John Howard
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 154pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

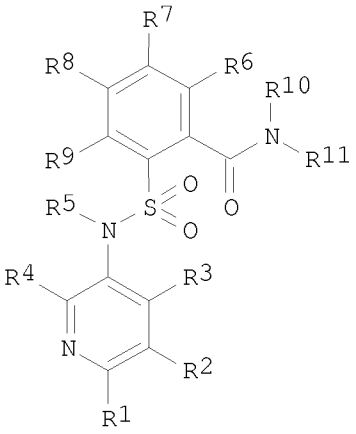
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007034312	A2	20070329	WO 2006-IB2639	20060911
WO 2007034312	A3	20070823		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 2007167497	A1	20070719	US 2007-621410	20070109

PRIORITY APPLN. INFO.:	US 2005-720151P	P	20050923
	US 2005-723115P	P	20051003
	US 2005-725469P	P	20051011
	US 2006-762256P	P	20060125
	US 2006-821664P	P	20060807
	WO 2006-IB2639	A1	20060911

OTHER SOURCE(S): MARPAT 146:379833

GI



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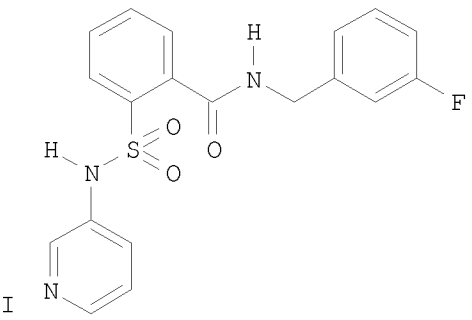
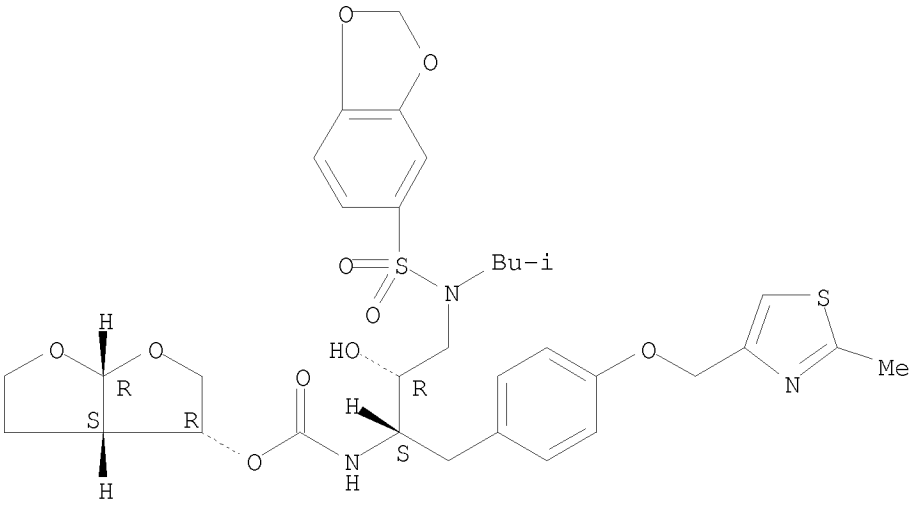


II

AB Title compds. I [R1-4 independently = H, alkyl, haloalkyl, etc.; R5 = H or alkyl; R6-9 independently = H, (un)substituted alkyl, heterocycloalkyl, etc.; R10 and R11 independently = H, (un)substituted alkyl, aryl, arylalkyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of cytochrome P 450 3A4. Thus, e.g., II was prepared by condensation of Me 2-(chlorosulfonyl)benzoate with 3-pyridinamine followed by amidation with 3-fluorobenzylamine. Assays were described for determining Kiapp of I against recombinant CYP3A4 enzyme, e.g., II was determined to have a Kiapp = 0.269 (μM). Further disclosed are methods for the use of I and pharmaceutical formulations comprising them.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug for therapeutic administration; preparation of pyridinylaminosulfonylarylcarboxamides as cytochrome P 450 3A4 inhibitors)
RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:350523 HCAPLUS
DOCUMENT NUMBER: 146:351294
TITLE: Methods for treating viral infections using polyamine analogs
INVENTOR(S): Mcgrath, Michael S.; Hadlock, Kenneth G.
PATENT ASSIGNEE(S): Pathologica, Llc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007035957	A2	20070329	WO 2006-US37378	20060925
WO 2007035957	A3	20070907		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,

MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 2007078187 A1 20070405 US 2006-535001 20060925
PRIORITY APPLN. INFO.: US 2005-719573P P 20050923

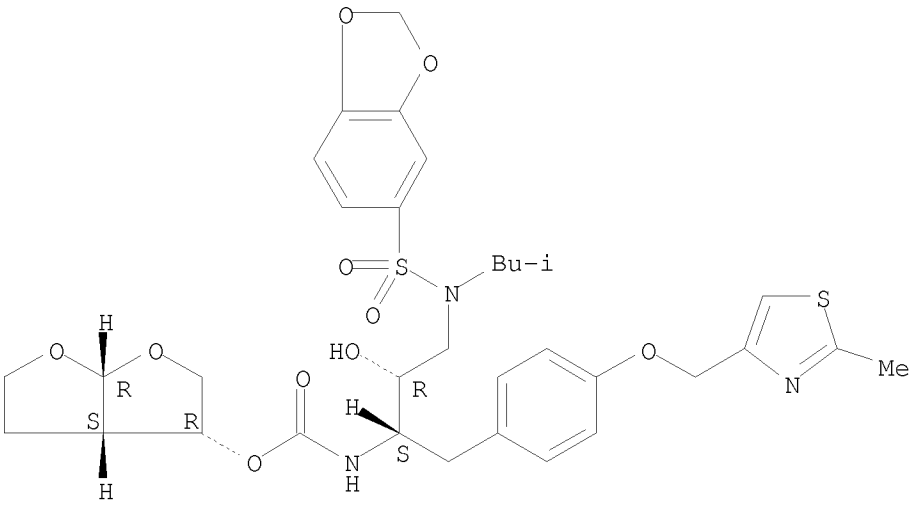
AB Methods for treating viral infections using polyamine analogs, including mitoguazone (MGBG), are provided. In these methods, polyamine analogs destroy macrophages that act as viral reservoirs, facilitating the destruction of the viruses that dwell within the macrophages. Examples of viral infections that may be treated with the methods include, but are not limited to, infections from human immunodeficiency viruses. These methods differ from previous methods of treatment using polyamine analogs, wherein the polyamine analogs were administered only as antitumor agents.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamine analogs for treatment of viral infections, and use with other agents)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:14210 HCAPLUS
DOCUMENT NUMBER: 146:121949
TITLE: Oxazolidinecarboxamides as HIV-1 protease inhibitors, and methods of making and using them

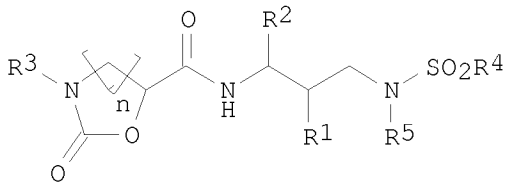
INVENTOR(S): Rana, Tariq M.; Ali, Akbar; Cao, Hong; Sai, Kiran Kumar Reddy Ga; Anjum, Saima Ghafoor
PATENT ASSIGNEE(S): University of Massachusetts, USA
SOURCE: PCT Int. Appl., 194pp., which which
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007002173	A1	20070104	WO 2006-US24109	20060621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-693134P P 20050622
US 2005-749902P P 20051212
US 2006-810234P P 20060602

OTHER SOURCE(S): MARPAT 146:121949
GI



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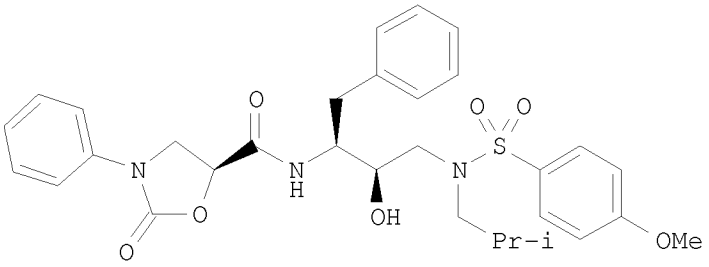


II

AB One aspect of the invention relates to the design, synthesis and biol. activity of novel HIV-1 protease inhibitors of incorporating N-phenyloxazolidine-5-carboxamides into the (hydroxyethylamino)sulfonamide scaffold of formula I as P2 ligands. Compound of formula I wherein n is 1

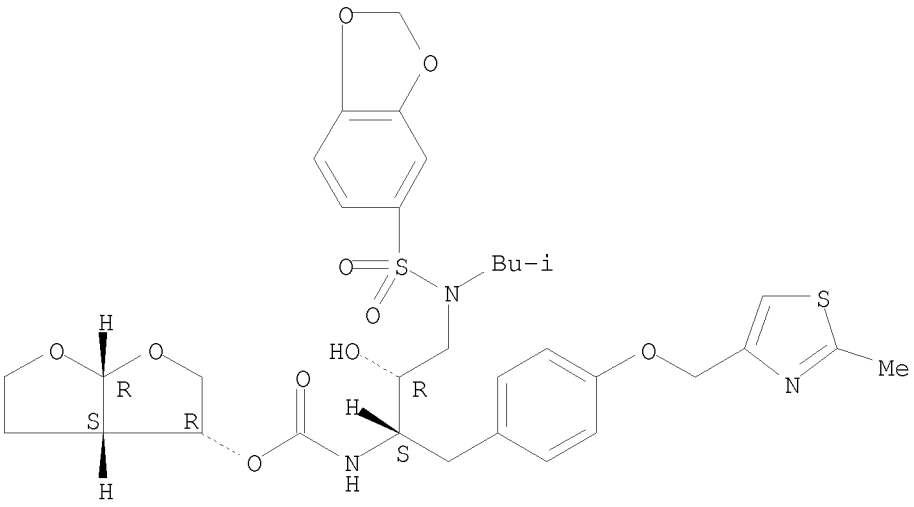
and 2; R1 is OH, SH, and NH and derivs.; R2 is H, alkyl, cycloalkyl, (hetero)aryl, heterocyclyl(alkyl), and (hetero)aralkyl; R3 is H, alkyl, alkenyl, aminoalkyl, amidoalkyl, ketoalkyl, cycloalkyl, (hetero)aryl, etc.; R4 is alkyl, cycloalkyl, heterocyclyl(alkyl), (hetero)aryl, and (hetero)aralkyl; R5 is H, alkyl, cycloalkyl, heterocyclyl(alkyl), (hetero)aryl, and (hetero)aralkyl; and their stereochem. configurations at any undefined stereocenter is R, S, or a mixture of these configurations, are claimed. The invention relates to inhibitors with variations at the P2 phenyloxazolidine and the P2' phenylsulfonamide moieties. Remarkably, compds. with an (S)-enantiomer of substituted phenyloxazolidines at P2 show highly potent inhibitory activities against wild-type HIV-1 protease. In certain embodiments, the inhibitors of the invention have Ki values in low picomolar (pM) range. In certain embodiments, the inhibitors of the invention were shown to be active against a variety of multi-drug resistant (MDR) HIV-1 proteases, each representing different paradigm of drug resistance. Example compound II was prepared by a general coupling reaction using the corresponding sulfonamide. All the invention compds. were evaluated for their HIV-1 protease inhibitory activity (data given).

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of oxazolidinecarboxamides as HIV-1 protease inhibitors useful as therapeutic agents)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:14194 HCAPLUS
DOCUMENT NUMBER: 146:114998

TITLE: HIV-1 protease inhibitors
INVENTOR(S): Schiffer, Celia; Rana, Tariq M.; Gilson, Michael; Tidor, Bruce
PATENT ASSIGNEE(S): University of Massachusetts, USA
SOURCE: PCT Int. Appl., 127pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007002172	A2	20070104	WO 2006-US24108	20060621
WO 2007002172	A3	20070405		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

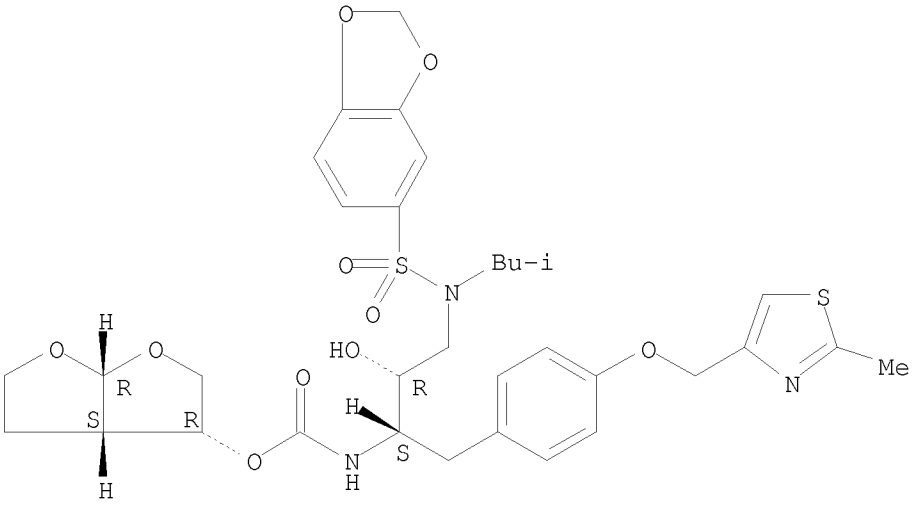
PRIORITY APPLN. INFO.: US 2005-693134P P 20050622
OTHER SOURCE(S): MARPAT 146:114998

AB Described are novel protease inhibitors and methods for using said protease inhibitors in the treatment of human immunodeficiency virus (HIV) infection.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV-1 protease inhibitors for treatment of human immunodeficiency virus infection and combination with other agents)

RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1030273 HCAPLUS
DOCUMENT NUMBER: 145:397501
TITLE: Substituted carbamates as HIV protease inhibitors and their preparation, pharmaceutical compositions and use in the treatment of HIV infection, AIDS and AIDS-related conditions
INVENTOR(S): Mclean, Ed, W.; Miller, John Franklin
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 73pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006104646	A1	20061005	WO 2006-US8102	20060307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1855672	A1	20071121	EP 2006-748311	20060307
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				

PRIORITY APPLN. INFO.: US 2005-660706P P 20050311

WO 2006-US8102 W 20060307

OTHER SOURCE(S): MARPAT 145:397501
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

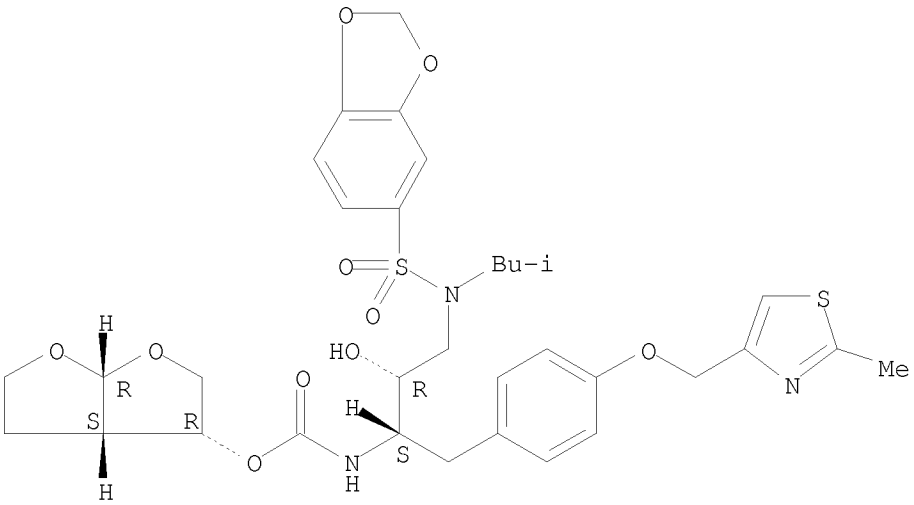
AB The invention features compds. of formula I that are HIV protease inhibitors and therefore are useful in the inhibition of HIV replication, the prevention and/or treatment of infection by HIV, and in the treatment of AIDS and/or ARC. Compds. of formula I wherein X is (un)substituted C1-5 alkylene; R1 is amino, C1-8 alkyl, C1-8 alkoxy, NR2, N(R2)2 and (un)substituted heterocycle; R2 is C1-8 alkyl and C1-8 alkoxy; and their pharmaceutically acceptable salts are claimed. Example compound II was prepared by in several steps (procedure given). All the invention compds. were evaluated for their HIV protease inhibitory activity. The key mean pharmacokinetic parameters, Cmax and AUC∞ values were determined to be < 1 ng/mL and < 1 ng/mL•hr, resp.

IT 313682-08-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of substituted carbamates as HIV protease inhibitors useful in treatment and prevention of HIV infection, AIDS and AIDS-related conditions)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



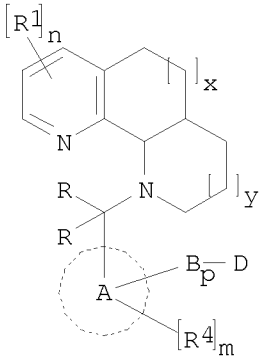
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:945669 HCAPLUS
DOCUMENT NUMBER: 145:336055
TITLE: Preparation of heteroarylmethyl substituted octahydro-1,10-phenanthrolines and analogs for treating diseases modulated by a chemokine receptor (CXCR4)
INVENTOR(S): Gudmundsson, Kristjan; Catalano, John, G.; Svolto, Angilique
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 183pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006096444	A2	20060914	WO 2006-US7395	20060301
WO 2006096444	A3	20070927		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 1853604	A2	20071114	EP 2006-736676	20060301
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: US 2005-658530P P 20050304
WO 2006-US7395 W 20060301
OTHER SOURCE(S): MARPAT 145:336055
GI



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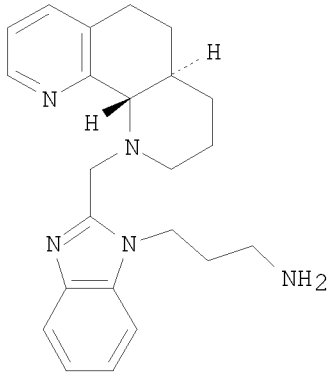


II

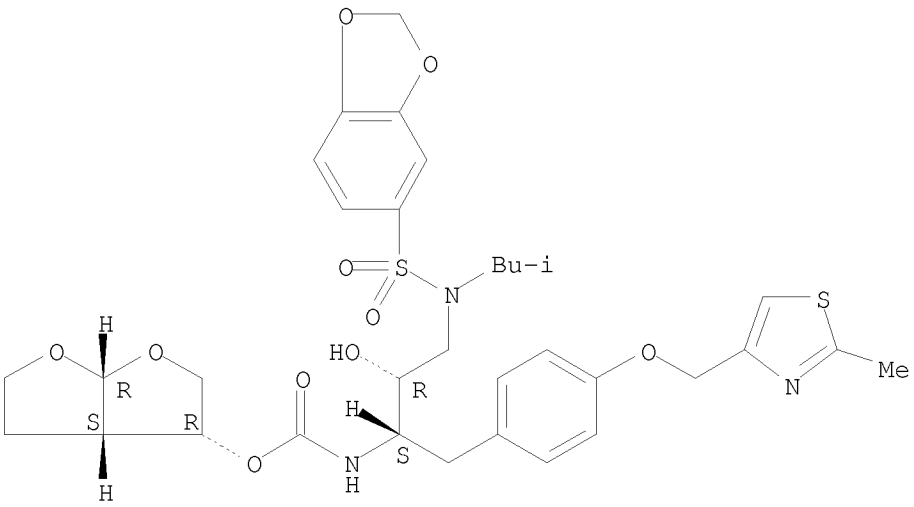
AB The title compds. I [x, y = 0-2; R = H, alkyl, haloalkyl, etc.; n = 0-3; R1 = halo, haloalkyl, alkyl, etc.; A = heteroaryl; R4 = halo, haloalkyl, alkyl, etc.; m = 0-2; p = 0-1; B = O, CO, CO2, etc.; D = N(R10)2, (un)substituted 4-6 membered heterocyclyl or heteroaryl; R10 = H, alkyl, cycloalkyl, etc.], useful in the treatment of diseases and conditions caused by CXCR4, were prepared E.g., a multi-step synthesis of trans-II, starting from 6,7-dihydro-8(5H)-quinolinone and acrylonitrile, was given. Compound I were tested in the HIV-1 infectivity assay (IC50 of about 1 nM to about 50 μM). Pharmaceutical formulations containing compds. I alone or in combination with other therapeutic agents are also disclosed.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of heteroarylmethyl substituted octahydro-1,10-phenanthrolines and their analogs for treating diseases modulated by a chemokine receptor (CXCR4))

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:722183 HCAPLUS

DOCUMENT NUMBER: 145:240783

TITLE: Inhibitors of HIV-1 protease: 10 years after

AUTHOR(S): Mastrolorenzo, Antonio; Rusconi, Stefano; Scozzafava, Andrea; Supuran, Claudiu T.

CORPORATE SOURCE: Dipartimento di Scienze Dermatologiche, Centro MTS, Universita degli Studi di Firenze, Florence, I-50121, Italy

SOURCE: Expert Opinion on Therapeutic Patents (2006), 16(8), 1067-1091

CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

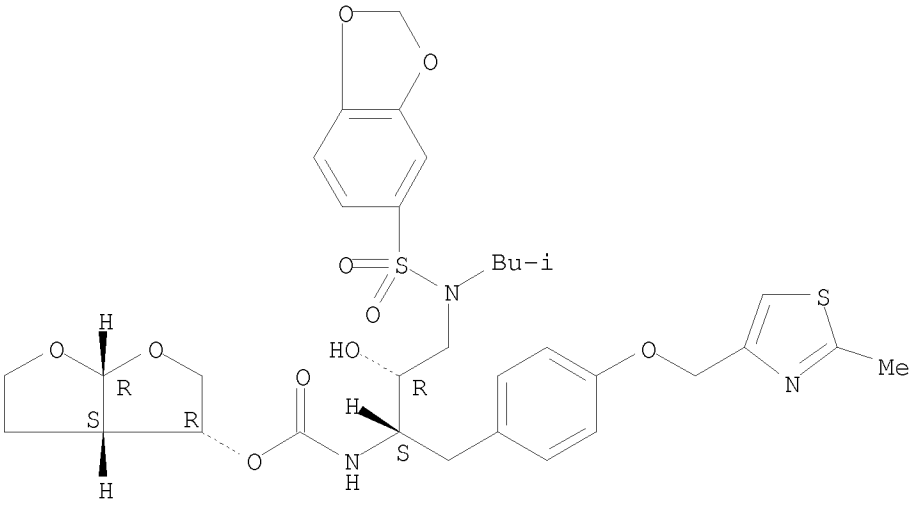
AB A review. Highly active antiretroviral therapy (HAART) has dramatically changed the course of HIV infection. This therapy involves the use of at least three agents from two distinct classes of antivirals: a protease inhibitor (PI) in combination with two nucleoside/nucleotide reverse transcriptase inhibitors (N(t)RTIs); or a non-nucleoside reverse transcriptase inhibitor (NNRTI) in combination with NRTIs. Nine drugs containing PIs are clin. available: the first-generation saquinavir, ritonavir, indinavir, nelfinavir and amprenavir; and the second-generation fosamprenavir (the amprenavir prodrug), lopinavir, atazanavir and tipranavir. Many other compds. are in advanced clin. evaluation, such as darunavir (TMC-114) and brecanavir, among others. Many other effective HIV PIs were reported, mainly by using amprenavir and TMC-114 as lead mols. The main goals of research in this field are: (i) the design of better pharmacol. agents, devoid of severe side effects, resistance problems and with simple administration schedules (preferably once-daily); and (ii) achieving eradication of the virus and, possibly, a definitive cure of the disease. A review of the pharmacol. and interactions of these agents with other drugs is presented here, with emphasis on how these pharmacol. interferences may improve the clin. use of antivirals, or how side effects due to PI drugs may be managed better by taking them into account (e.g., ritonavir boosting of other PIs, which reduces dosages and administration schedules of these drugs). Except for being highly effective in the treatment of HIV infection, recent reports showed this class of drugs to be effective as antitumor agents, apoptosis enhancers, antibacterials (e.g., against Mycobacterium tuberculosis infection), antifungals (e.g., against Candida albicans), antimalarials, anti-SARS and anti-influenza agents.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of HIV-1 protease and anti-AIDS therapy)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:633928 HCAPLUS
DOCUMENT NUMBER: 145:103723
TITLE: Preparation of hydroxydihydropyridopyrazine-1,8-diones for inhibiting HIV integrase
INVENTOR(S): Chan Chun Kong, Laval; Liu, Bingcan; Nguyen-Ba, Nghe; Cadilhac, Caroline; Turcotte, Nathalie
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 186 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

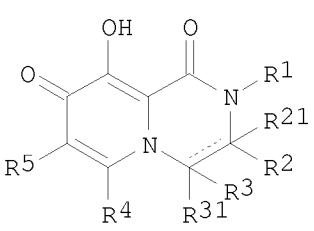
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006066414	A1	20060629	WO 2005-CA1964	20051222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

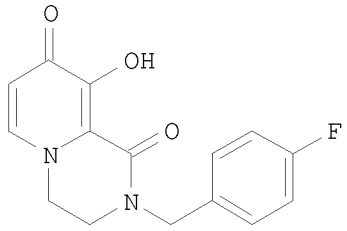
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-638180P P 20041223
OTHER SOURCE(S): MARPAT 145:103723

GI



I



II

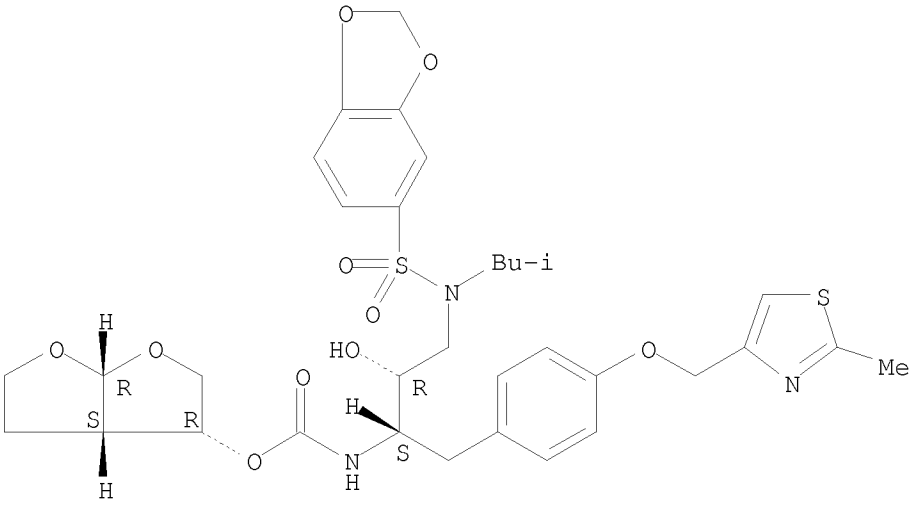
AB The title compds. I [R1 = H, OH, (un)substituted aryl, etc.; R2, R21, R3, R31 = H, (un)substituted alkyl, cycloalkyl, etc.; or two of R2, R21, R3 and R31 can be joined to form a condensed or spiro ring; or R2 and R21 or R3 and R31 can also be joinned together to form a carbonyl; R4 = (un)substituted alkoxy, aryloxy, arylalkoxy; R5 = H, halo, OH, etc.], useful for preventing or treating human immunodeficiency virus (HIV) infection or for preventing, delaying or treating acquired immunodeficiency syndrome (AIDS), were prepared E.g., a multi-step synthesis of II, starting from 3-methoxy-2-methyl-1H-pyridone, was given. Compds. I have been found to have activity in the inhibition of HIV integrase, generally with an observed inhibitory activity at 50 μM. Certain compds. I have also been tested in an assay for HIV activity and generally having an IC50 value of less than 10 μM. Pharmaceutical compns. comprising the compound I alone or in combination with other therapeutic agents are disclosed.

IT 313682-08-5, VX 385
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of hydroxydihydropyridopyrazinediones as HIV integrase inhibitors for treating, preventing or delaying HIV infection and AIDS)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

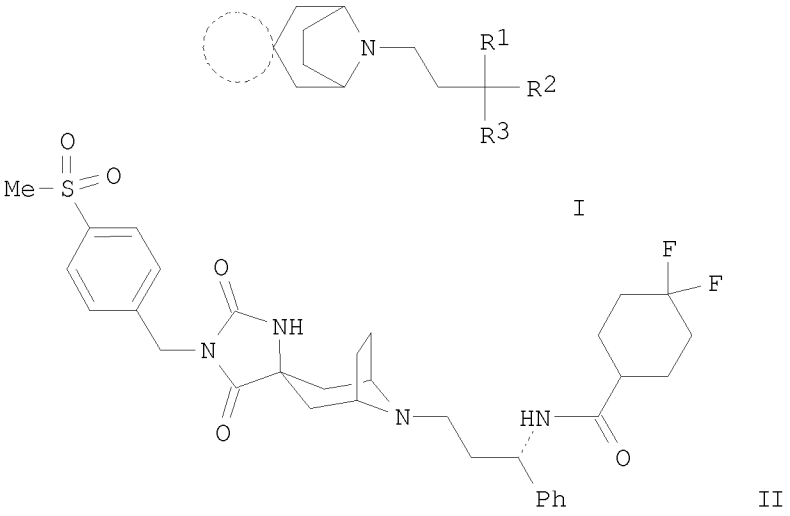
L14 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:578211 HCAPLUS
DOCUMENT NUMBER: 145:62897
TITLE: Preparation of spirotropane compounds and therapeutic use as modulators of chemokine receptor activity
INVENTOR(S): Chan Chun Kong, Laval; Moinet, Christophe; Courchesne, Marc; Vaillancourt, Louis; Blais, Charles; Bubenik, Monica
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060919	A1	20060615	WO 2005-CA1878	20051209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005313813	A1	20060615	AU 2005-313813	20051209
CA 2587508	A1	20060615	CA 2005-2587508	20051209

EP 1831222	A1	20070912	EP 2005-819431		20051209
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU					
CN 101098871	A	20080102	CN 2005-80046172		20051209
IN 2007KN02150	A	20070817	IN 2007-KN2150		20070612
KR 2007095310	A	20070928	KR 2007-715147		20070702
PRIORITY APPLN. INFO.:			US 2004-634266P	P	20041209
			US 2005-693051P	P	20050623
			WO 2005-CA1878	W	20051209

OTHER SOURCE(S): CASREACT 145:62897; MARPAT 145:62897

GI



I

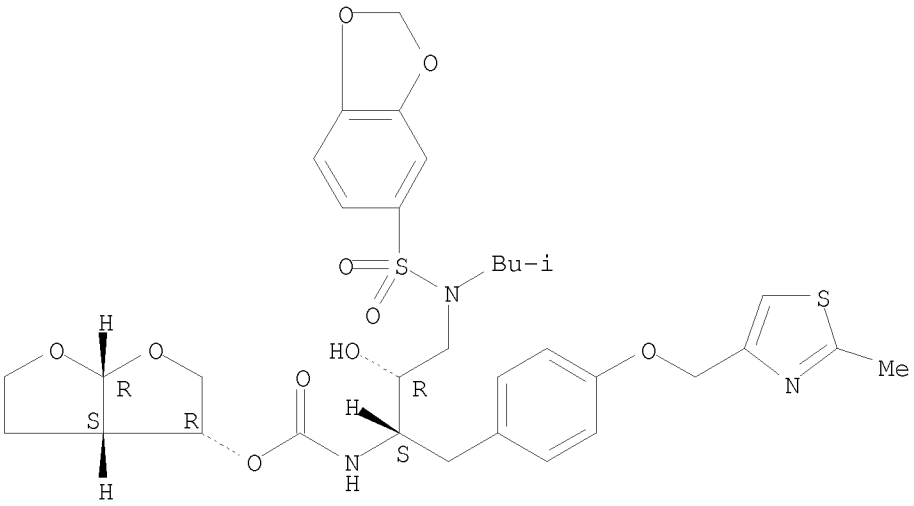
II

AB Spiro compds. according to formula (I) are claimed: wherein R1 = NR7R9; R2 = (un)substituted C1-10 alkyl, C2-10 alkenyl, 3-10 membered heterocycle, etc.; R3 = H, (un)substituted C1-10 alkyl or C6-12 aryl; R7 = H, (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl; R9 = H or (un)substituted C1-10-alkyl; and ring A represents a 5 or 6 membered heteroring substituted once or twice with a keto substituent. These compds. and their pharmaceutical acceptable salts are used in combinations or in pharmaceutical compns. and are useful in the modulation of CCR5 chemokine receptor activity (no data given). I are useful in the prevention or treatment of certain inflammatory diseases, immunoregulatory diseases, organ transplantation reactions and in the prevention and treatment of infectious diseases such as HIV infections. Preparation of I is exemplified. For example, II was prepared from 4,4-difluorocyclohexanecarboxylic acid ((S)-3-oxo-1-phenylpropyl)amide and 3-(4-methanesulfonylbenzyl)bicyclo[3.2.1]-1α,3,8-triazaspiro[4.5]dodecan-2,4-dione hydrochloride (preparation given).

IT 313682-08-5, VX 385
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addnl. therapeutic agent; preparation of spirotropane compds. and

therapeutic use as modulators of chemokine receptor activity)
RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:558325 HCAPLUS
DOCUMENT NUMBER: 145:62894
TITLE: Preparation of spirotropane compounds and methods for the modulation of chemokine receptor activity to block cellular entry of HIV
INVENTOR(S): Chan Chun Kong, Laval; Moinet, Christophe; Courchesne, Marc; Vaillancourt, Louis; Bubenik, Monica
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060918	A1	20060615	WO 2005-CA1877	20051209

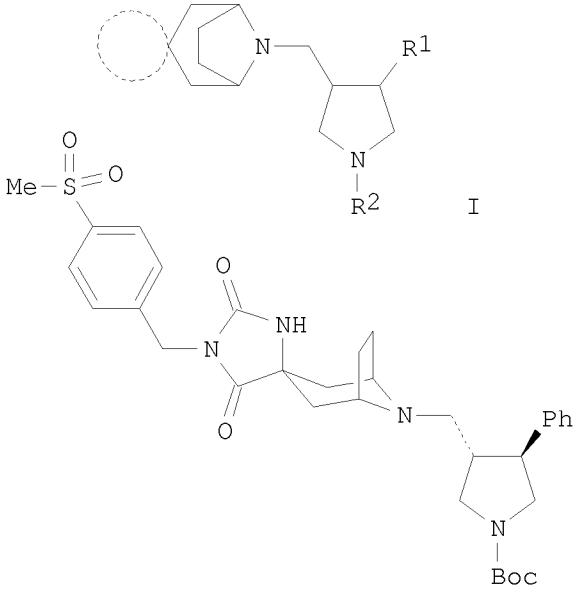
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,

VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

CA 2590737	A1	20060615	CA 2005-2590737		20051209
EP 1824853	A1	20070829	EP 2005-819950		20051209
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU					
PRIORITY APPLN. INFO.:			US 2004-634257P	P	20041209
			WO 2005-CA1877	W	20051209

OTHER SOURCE(S): MARPAT 145:62894

GI



AB Compds. according to formula I (wherein the R1= (un)substituted alkyl, alkenyl, etc.; R2 = H, cycloalkylcarbonyl, ester, etc.; and A = a 5 or 6 membered heteroring involving a nitrogen or oxygen atom and one or two keto substituent) are claimed. These compds. and their pharmaceutical acceptable salt are used in combinations or pharmaceutical compns. and are useful in modulation of CCR5 chemokine receptor activity and blocking cellular entry of HIV (no biol. data given). Preparation of I is exemplified. For example, II was prepared from 3-(4-methanesulfonylbenzyl)bicyclo[3.2.1]-1a,3,8-triazaspiro[4.5]dodecan-2,4-dione hydrochloride (preparation given) and (3R,4S)-3-formyl-4-phenylpyrrolidine-1-carboxylic acid tert-Bu ester (preparation given).

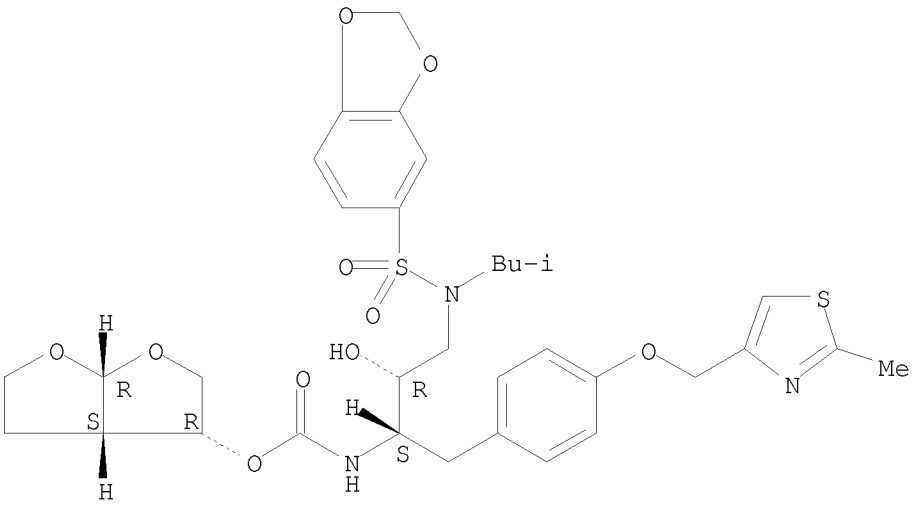
IT 313682-08-5, VX 385
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(addnl. therapeutic agent; preparation of spirotropane compds. and methods for modulation of chemokine receptor activity to block cellular entry of HIV)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:547194 HCAPLUS

DOCUMENT NUMBER: 145:55430

TITLE: Single-dose safety and pharmacokinetics of brecanavir, a novel human immunodeficiency virus protease inhibitor

AUTHOR(S): Ford, Susan L.; Reddy, Y. Sunila; Anderson, Maggie T.; Murray, Sharon C.; Fernandez, Pedro; Stein, Daniel S.; Johnson, Mark A.

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(6), 2201-2206
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Brecanavir (BCV, 640385) is a novel, potent protease inhibitor (PI) with low nanomolar 50% inhibitory concns. against PI-resistant human immunodeficiency virus (HIV) in vitro. This phase I, double-blind, randomized, placebo-controlled, two-part single-dose study (first time with humans) was conducted to determine the safety, tolerability, and pharmacokinetics of BCV administered at 10 mg/mL in a tocopherol-polyethylene glycol succinate-polyethylene glycol 400-ethanol 50:40:10

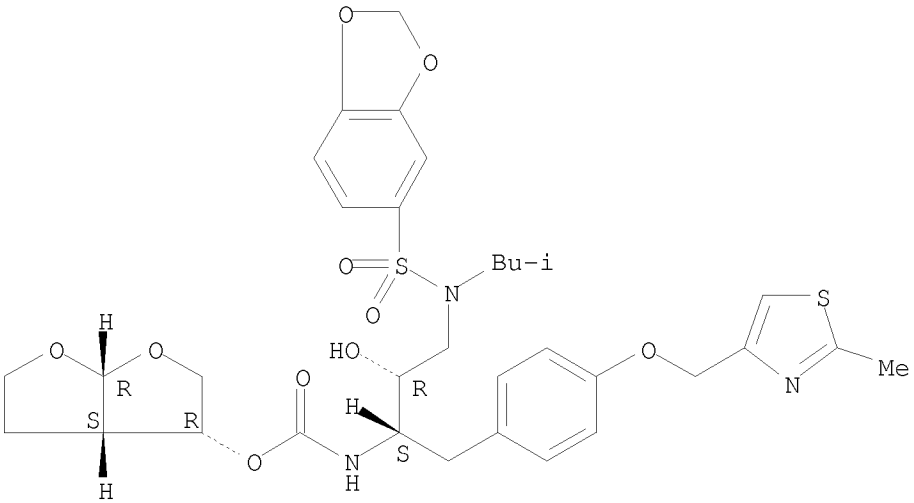
solution In part 1 of the study, single oral doses of BCV ranged from 25 mg to 800 mg. In part 2, single oral doses of BCV ranged from 10 mg to 300 mg and were coadministered with 100-mg oral ritonavir (RTV) soft gel capsules. Single doses of BCV and BCV/RTV were generally well tolerated. There were no severe adverse events (SAEs), and no subject was withdrawn due to BCV. The most commonly reported drug-related AEs during both parts of the study combined were gastrointestinal disturbances (similar to placebo) and headache. BCV was readily absorbed following oral administration with mean times to maximum concentration from >1 h to 2.5 h in part 1
and from 1.5 h to 3 h in part 2. Administration of BCV without RTV resulted in BCV exposures predicted to be insufficient to inhibit PI-resistant virus based on in vitro data. Coadministration of 300 mg BCV with 100 mg RTV, however, significantly increased the plasma BCV area under the concentration-time curve and maximum concentration 26-fold and 11-fold, resp.,
achieving BCV concns. predicted to inhibit PI-resistant HIV.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single-dose safety and pharmacokinetics of brecanavir, a novel human immunodeficiency virus protease inhibitor)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:456993 HCAPLUS
DOCUMENT NUMBER: 144:474844
TITLE: Conjugates with enhanced cell uptake activity

INVENTOR(S): Bonny, Christophe; Coquoz, Didier; Chen, Jianhua
PATENT ASSIGNEE(S): Xigen S.A., Switz.
SOURCE: Eur. Pat. Appl., 65 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

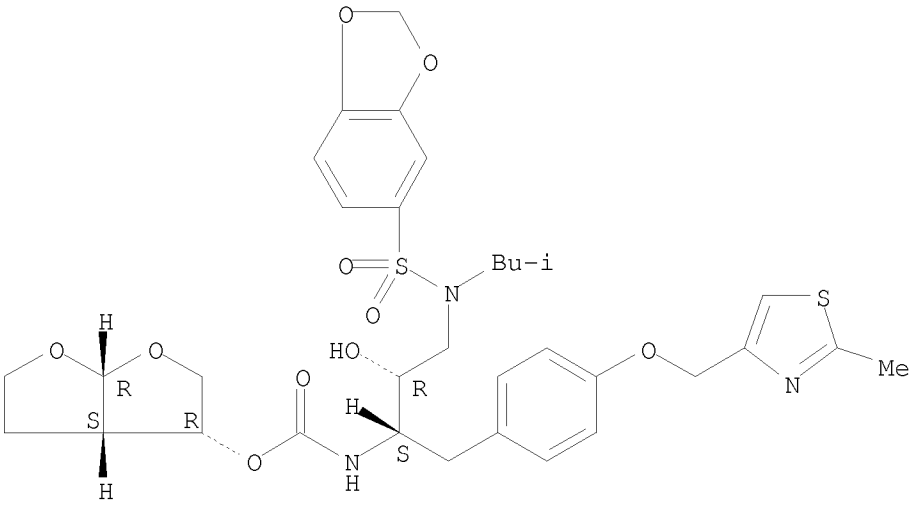
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1656951	A1	20060517	EP 2004-26934	20041112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
AU 2005303949	A1	20060518	AU 2005-303949	20051109
CA 2585421	A1	20060518	CA 2005-2585421	20051109
WO 2006050930	A2	20060518	WO 2005-EP11991	20051109
WO 2006050930	A3	20070426		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 1809334	A2	20070725	EP 2005-811041	20051109
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 101072589	A	20071114	CN 2005-80038728	20051109
PRIORITY APPLN. INFO.:			EP 2004-26934 A	20041112
			WO 2005-EP11991 W	20051109

AB This invention relates to a conjugate mol. comprising at least one first portion (I) comprising a carrier sequence and at least one second portion (II) comprising at lest one anti-tumor drug mol. or a protease inhibitor mol., said conjugate mol. comprising D-enantiomeric amino acids in its portion (I). Furthermore, the invention relates to pharmaceutical compns. containing said conjugate mol. as well as to the use of said conjugate mol. for therapeutical treatment. Methods for improving cell permeability are disclosed as well.

IT 313682-08-5, Proteinase Inhibitor 640385
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Vertex 385; D-enantiomeric peptide conjugates with enhanced cell uptake activity)

RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:367270 HCAPLUS
DOCUMENT NUMBER: 144:398367
TITLE: Amorphous pharmaceutical compositions comprising rosiglitazone
INVENTOR(S): Ignatious, Francis; Sun, Linghong; Craig, Andrew; Crowe, David; Ho, Tim; Millan, Michael
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 523,835.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006083784	A1	20060420	US 2005-64890	20050224
WO 2004014304	A2	20040219	WO 2003-US24641	20030807
WO 2004014304	A3	20040624		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006013869	A1	20060119	US 2005-523835	20050207

WO 2006090150 A1 20060831 WO 2006-GB632 20060223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
EP 1853262 A1 20071114 EP 2006-709864 20060223
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR
IN 2007DN06569 A 20070921 IN 2007-DN6569 20070824
KR 2007112217 A 20071122 KR 2007-721885 20070921
PRIORITY APPLN. INFO.: US 2002-401726P P 20020807
WO 2003-US24641 W 20030807
US 2005-523835 A2 20050207
US 2005-64890 A 20050224
WO 2006-GB632 W 20060223

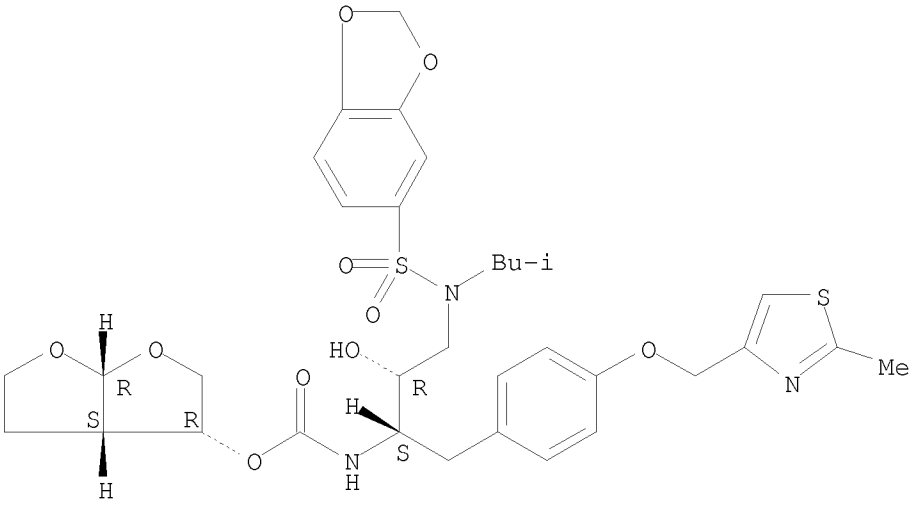
AB The present invention is directed to use of electrospinning, i.e. the process of making polymer nanofibers from either a solution or melt under elec. forces, to prepare stable, solid dispersions of amorphous drugs in polymer nanofibers. The present invention is also directed to the process of making solid dispersions of amorphous forms and compns. of rosiglitazone and its pharmaceutically acceptable salts. A 3.1 weight% solution of rosiglitazone mesylate 2-PrOH-water was spray dried to give an amorphous powder.

IT 313682-08-5
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous pharmaceutical compns. comprising rosiglitazone)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:319029 HCAPLUS
DOCUMENT NUMBER: 144:370090
TITLE: Aminotetrahydroquinolines as cytoprotectants from HIV infection, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Gudmundsson, Kristjan; Boggs, Sharon Davis
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006036816	A2	20060406	WO 2005-US34218	20050923
WO 2006036816	A3	20060615		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1793825	A2	20070613	EP 2005-817347	20050923
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR				

PRIORITY APPLN. INFO.: US 2004-612844P P 20040924

WO 2005-US34218 W 20050923

OTHER SOURCE(S): MARPAT 144:370090

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

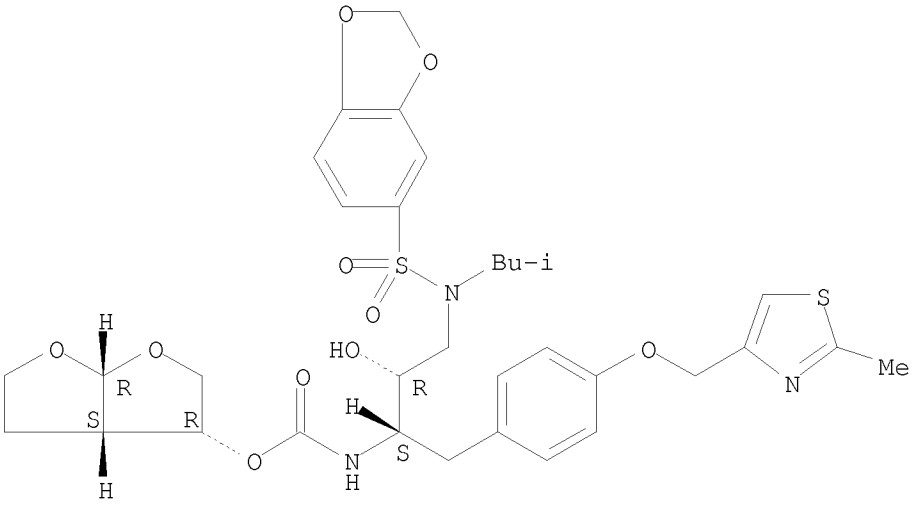
AB The invention relates to compds. of general formula I, which demonstrate protective effects on target cells from HIV infection in a manner as to bind specifically to the chemokine receptor, and which affect the binding of the natural ligand or chemokine to a receptor such as CXCR4 and/or CCR5 of a target cell. In compds. I, p is 0-2; each R1 is independently selected from halo, alkyl, haloalkyl, alkenyl, cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, etc.; n is 0-2; each R2 is independently selected from H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, etc.; R3 is selected from H, halo, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, etc.; each R4 is independently selected from halo, cyano, nitro, alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, etc.; m is 0-2; Y is (un)substituted alkylene, (un)substituted cycloalkylene, alkenylene, cycloalkenylene, or alkynylene; and Z is (un)substituted amino, (un)substituted aminoaryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, etc.; including pharmaceutically acceptable salts and esters thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, optionally containing one or more addnl. therapeutic agents, as well as to the use of the compns. for the prevention of infection of a cell by HIV. Reductive amination of quinolinone II with tert-Bu N-(4-aminobutyl)carbamate and reductive amination with 5-fluoroimidazo[1,2-a]pyridine-2-carboxaldehyde gave amine III, which underwent substitution with tert-Bu piperazine-1-carboxylate and deprotection to give aminotetrahydroquinoline IV. Several compds. of the invention show HIV anti-infective activity, e.g., compound IV expresses activity of 2.2 nM in an HOS HIV-1 anti-infectivity assay.

IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of aminotetrahydroquinolines as cytoprotectants from HIV infection)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.

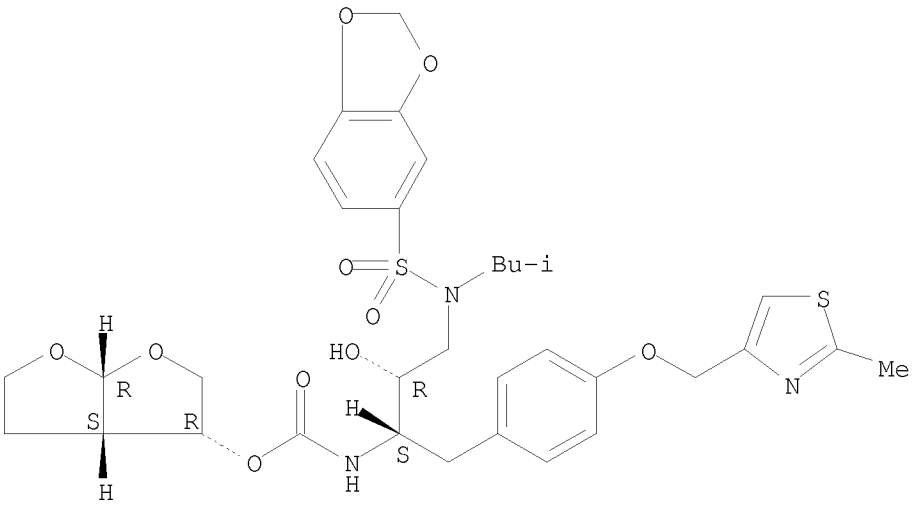


L14 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:270625 HCAPLUS
DOCUMENT NUMBER: 144:266487
TITLE: Discovery of next generation inhibitors of HIV protease
AUTHOR(S): Spaltenstein, Andrew; Kazmierski, Wieslaw M.; Miller, John F.; Samano, Vicente
CORPORATE SOURCE: Division of Chemistry, MV CEDD, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Current Topics in Medicinal Chemistry (Sharjah, United Arab Emirates) (2005), 5(16), 1589-1607
CODEN: CTMCCL; ISSN: 1568-0266
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Due to factors such as resistance and long-term side effects as well as dosing regimen-related adherence issues, HIV therapy is a constantly moving target. HIV-1 protease inhibitors had an immediate and dramatic impact on the outcome of HIV/AIDS when launched in late 1995, and the search for new and improved next generation mols. has been under way in many labs. At GlaxoSmithKline (GSK) and Vertex Pharmaceuticals, this effort focused on 2 key issues, patient compliance and viral resistance. Using a water-solubilizing prodrug approach, the pill burden in delivering a protease inhibitor, Amprenavir, was dramatically decreased. By eliminating the large amts. of excipients necessary for the original soft-gel formulation, Fosamprenavir (Lexiva/Telzir) delivers the clin. efficacious dose of Amprenavir with 2 compact tablets per dose, compared to 8 gel capsules. The efforts to overcome viral resistance to 1st generation protease inhibitors by further elaborating the SAR of the Amprenavir and related scaffolds led to successive and dramatic improvements in wild-type antiviral potencies, and ultimately to the discovery of ultra-potent mols. with very favorable overall resistance profiles. The selection of GW640385 (Brecanavir - USAN approved only) as a clin. candidate and its progression into current phase 2 dose ranging studies represents the culmination of the effort toward the next

generation protease inhibitors.
IT 313682-08-5, Brecanavir
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of next generation inhibitors of HIV protease)
RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.

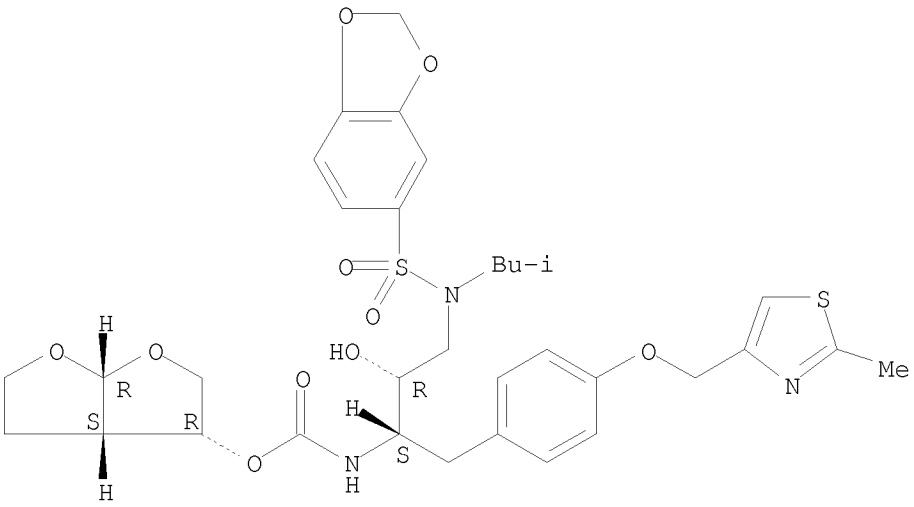


REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:252581 HCAPLUS
DOCUMENT NUMBER: 144:425067
TITLE: In vitro development of resistance to human immunodeficiency virus protease inhibitor GW640385
AUTHOR(S): Yates, P. J.; Hazen, R.; St. Clair, M.; Boone, L.; Tisdale, M.; Elston, R. C.
CORPORATE SOURCE: GlaxoSmithKline Inc., Stevenage, UK
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(3), 1092-1095
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Development of in vitro resistance to GW640385, a new human immunodeficiency virus type 1 protease inhibitor, was studied. Variants characterized included one with <4-fold resistance and amino acid substitutions Q58E/A71V (protease) and P452K (Gag) and one with >50-fold resistance and amino acid substitutions L10F/G16E/E21K/A28S/M46I/F53L/A71V (protease) and L449F/P453T (Gag). The A28S substitution substantially reduced replication capacity.

IT 313682-08-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro development of resistance to human immunodeficiency virus protease inhibitor GW640385)
RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:188865 HCAPLUS
DOCUMENT NUMBER: 144:432712
TITLE: Ultra-potent P1 modified arylsulfonamide HIV protease inhibitors: The discovery of GW0385
AUTHOR(S): Miller, John F.; Andrews, C. Webster; Brieger, Michael; Furfine, Eric S.; Hale, Michael R.; Hanlon, Mary H.; Hazen, Richard J.; Kaldor, Istvan; McLean, Ed W.; Reynolds, David; Sammond, Douglas M.; Spaltenstein, Andrew; Tung, Roger; Turner, Elizabeth M.; Xu, Robert X.; Sherrill, Ronald G.
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(7), 1788-1794
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:432712
AB A novel series of P1 modified HIV protease inhibitors was synthesized and evaluated for in vitro antiviral activity against wild-type virus and

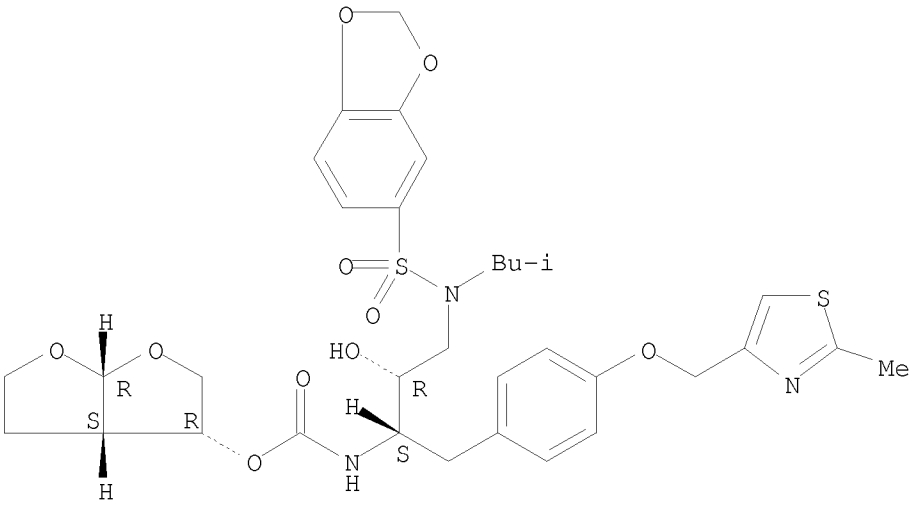
protease inhibitor-resistant viruses. Optimization of the P1 moiety resulted in compds. with femtomolar enzyme activities and cellular antiviral activities in the low nanomolar range culminating in the identification of clin. candidate GW0385.

IT 313682-08-5P, GW0385
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of the dioxabicyclooctyl thiazolylmethoxybenzyl-substituted (benzodioxolylsulfonylamino)propylcarbamate GW0385 as an anti-HIV agent and its pharmacokinetics and behavior in resistant HIV strains)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:698347 HCAPLUS
DOCUMENT NUMBER: 143:194248
TITLE: Therapeutic combinations containing an amino acid amide HIV protease inhibitor
INVENTOR(S): Hammond, Jennifer Lou; Patick, Amy Karen
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2005171038	A1	20050804	US 2005-46260		20050128
AU 2005216710	A1	20050909	AU 2005-216710		20050117
CA 2555171	A1	20050909	CA 2005-2555171		20050117
WO 2005082362	A1	20050909	WO 2005-IB101		20050117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

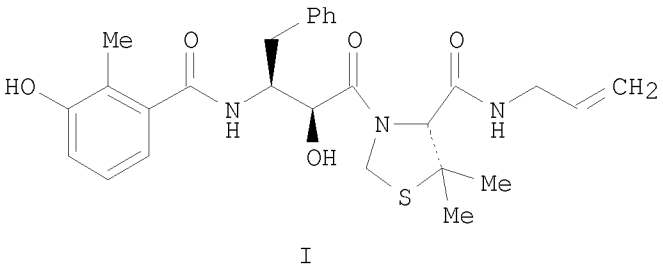
EP 1713470	A1	20061025	EP 2005-702264		20050117

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS

BR 2005006493	A	20070213	BR 2005-6493		20050117
CN 1938017	A	20070328	CN 2005-80010030		20050117
JP 2007519704	T	20070719	JP 2006-550331		20050117
NO 2006003483	A	20060830	NO 2006-3483		20060731
MX 2006PA08632	A	20060904	MX 2006-PA8632		20060731
IN 2006DN04522	A	20070824	IN 2006-DN4522		20060804
PRIORITY APPLN. INFO.:			US 2004-540749P	P	20040130
			US 2004-615000P	P	20041001
			WO 2005-IB101	W	20050117

OTHER SOURCE(S): CASREACT 143:194248

GI



I

AB The invention is related to methods for treating an HIV infection by using a therapeutically effective amount of a combination of compds., including I and its related N-amide derivs. The invention is also related to compns. comprising certain compds. useful as inhibitors of the HIV protease enzyme and at least one addnl. therapeutic agent. In an XTT dye reduction method, I in combination with ritonavir acted synergistically against HIV-1 infection.

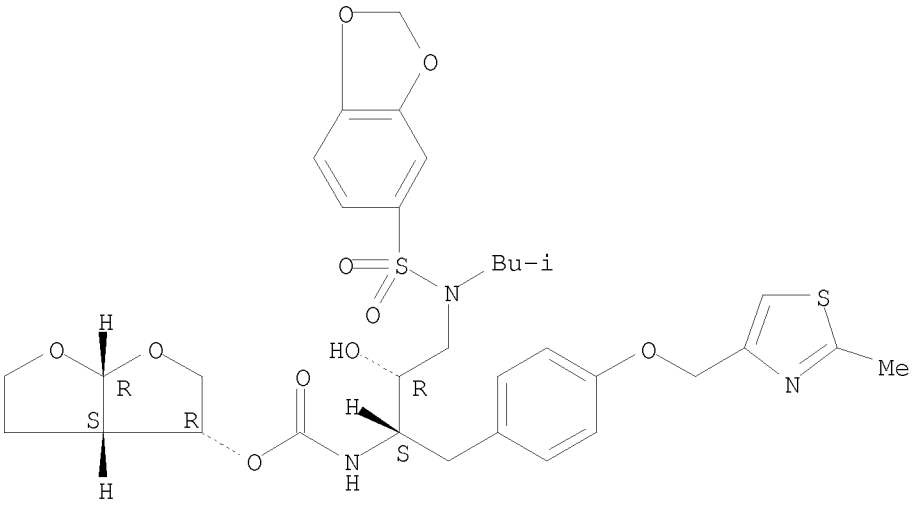
IT 313682-08-5, VX 385
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combination therapy agent; compns. comprising an amino acid amide HIV protease inhibitor)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-

thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

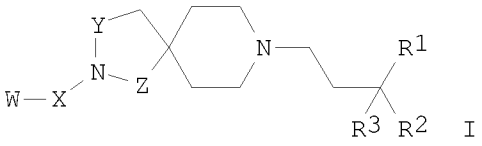
Absolute stereochemistry.



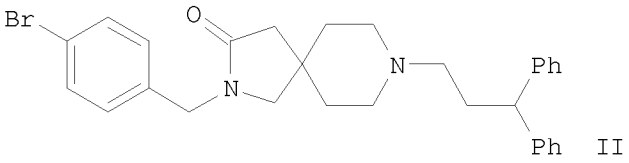
L14 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:74120 HCAPLUS
DOCUMENT NUMBER: 142:176697
TITLE: Preparation of spiro compounds for the modulation of chemokine receptor activity
INVENTOR(S): Chan, Chun Kong; Zhang, Ming-Qiang; Moinet, Christophe; Proulx, Melanie; Reddy, Thumkunta Jagadeeswar; Courchesne, Marc
PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 338 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007656	A1	20050127	WO 2004-CA1048	20040716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2573951	A1	20050127	CA 2004-2573951	20040716

EP 1776362 A1 20070425 EP 2004-761573 20040716
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LT, LV, MK
US 2005075326 A1 20050407 US 2004-893583 20040719
PRIORITY APPLN. INFO.: US 2003-487973P P 20030718
WO 2004-CA1048 W 20040716
OTHER SOURCE(S): MARPAT 142:176697
GI



I



II

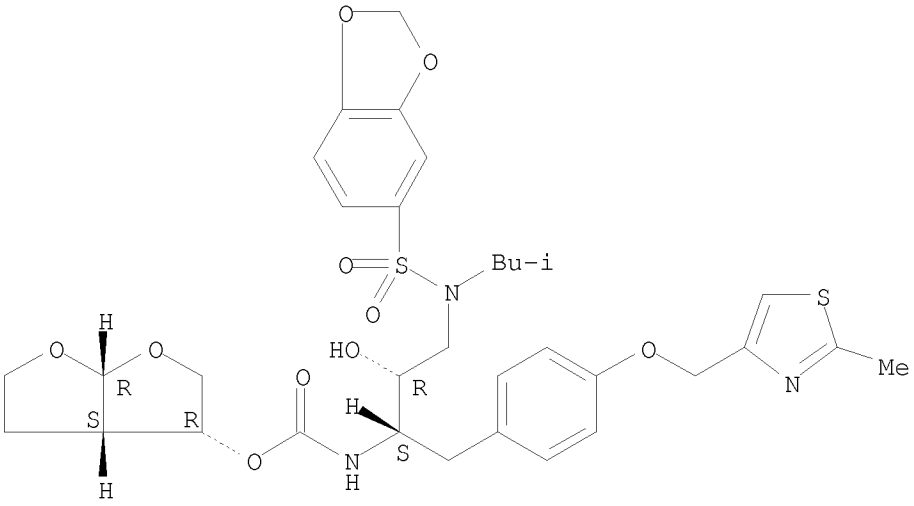
AB The title compds. I [Y, Z and X = CH2, CO, CR4R5; W = H, alkyl, alkenyl, aryl, etc.; R1 = H, OH, alkyl, etc.; R2 = alkyl, alkenyl, alkynyl, aryl, heterocyclyl; R3 = H, alkyl, alkenyl, alkynyl, aryl; R4, R5 = H, alkyl, alkenyl, alkynyl, aryl] and their pharmaceutically acceptable salts, useful for the modulation of CCR5 chemokine receptor activity and the treatment or prevention of diseases associated therewith, were prepared E.g., a multi-step synthesis of II.HCl, starting from tert-Bu 1-oxo-2,8-diaza-spiro[4.5]decane-8-carboxylate and 4-bromobenzyl bromide, was given. The compds. I have been found to have activity in binding to the CCR5 receptor, generally with an IC50 values of < 25 μM. Certain compds. I have also been tested in an assay for HIV activity, and generally having an IC50 values of < 1 μM.

IT 313682-08-5, VX 385
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of spiro compds. for treating diseases associated with CCR5 chemokine receptor activity in combination with other agents)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:14172 HCAPLUS
DOCUMENT NUMBER: 142:114047
TITLE: A preparation of furofuranyl derivative, useful as inhibitor of HIV aspartyl protease
INVENTOR(S): Roberts, John Charles; Toczko, Jennifer Fell
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; Martin, Michael Tolar
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000249	A2	20050106	WO 2004-US20353	20040625
WO 2005000249	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1638960	A2	20060329	EP 2004-777060	20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				

JP 2007521277	T	20070802	JP 2006-517643		20040625
US 2006148865	A1	20060706	US 2005-560500		20051212
PRIORITY APPLN. INFO.:			US 2003-483002P	P	20030627
			WO 2004-US20353	W	20040625

OTHER SOURCE(S): CASREACT 142:114047
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

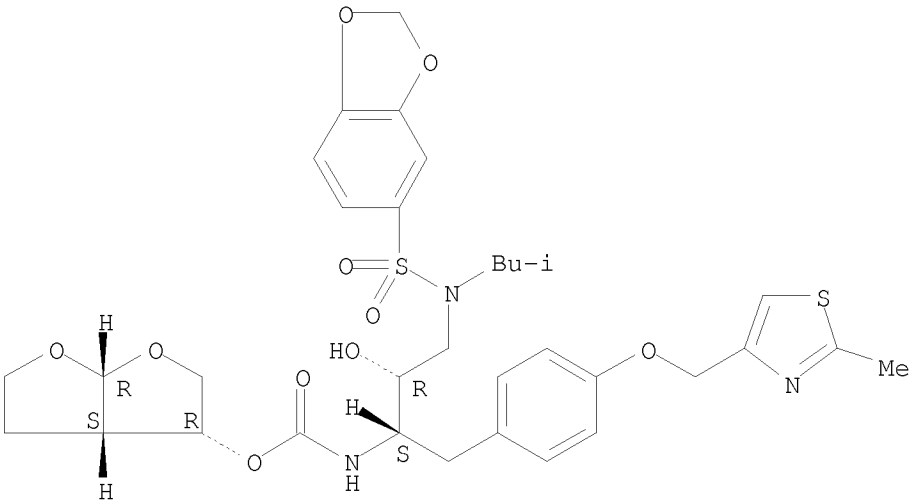
AB The invention relates to a preparation of furofuranyl derivative I, useful as inhibitor of HIV aspartyl protease (no biol. data). For instance, I was prepared via deprotection of II and coupling with III with a yield of 90% (example 2).

IT 313682-08-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



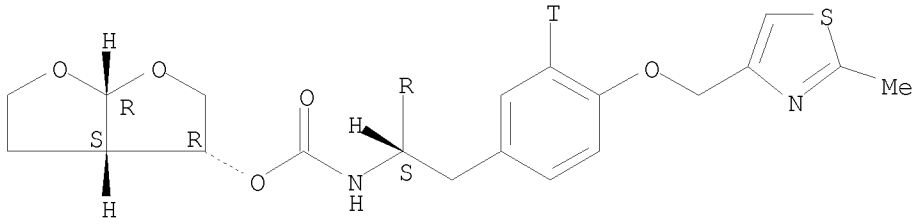
L14 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2004:885959 HCAPLUS
DOCUMENT NUMBER:	142:51214
TITLE:	Inhibition of Wild-Type and Mutant Human Immunodeficiency Virus Type 1 Proteases by GW0385 and Other Arylsulfonamides
AUTHOR(S):	Hanlon, Mary H.; Porter, David J. T.; Furfine, Eric

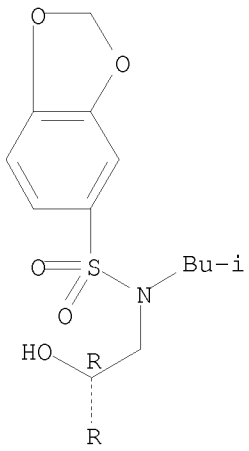
S.; Spaltenstein, Andrew; Carter, H. Luke; Danger, Dana; Shu, Arthur Y. L.; Kaldor, Istvan W.; Miller, John F.; Samano, Vicente A.
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, PA, 19405, USA
SOURCE: Biochemistry (2004), 43(45), 14500-14507
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The arylsulfonamide derivs. described herein were such potent inhibitors of human immunodeficiency virus type 1 (HIV-1) protease (enzyme, E) that values for the inhibition consts. (Ki) could not be determined by conventional steady-state kinetic techniques (i.e., the minimal enzyme concentration usable for the activity assay was much greater than the value of the dissociation constant). Consequently, two alternative methods were developed for estimation of Ki values. The first method employed kinetic detns. of values for k1 and k-1, from which Ki was determined (k-1/k1). The second method was a competitive displacement assay used to determine binding affinities of other inhibitors relative to that of GW0385. In these assays, the inhibitor of unknown affinity was used to displace [3H]GW0385 from E·[3H]GW0385. From the concentration of E·[3H]GW0385 at equilibrium, the concns. of enzyme-bound and free inhibitors were calculated, and the ratio of the Ki value of the unknown to that of GW0385 was determined (Ki,unknown/Ki,GW0385). The values of k1 were calculated from data in which changes in the intrinsic protein fluorescence of the enzyme associated with inhibitor binding were directly or indirectly monitored. In the case of saquinavir, the fluorescence changes associated with complex formation were large enough to monitor directly. The value of k1 for saquinavir was 62±2 μM-1 s-1. In the case of GW0385, the fluorescence changes associated with complex formation were too small to monitor directly. Consequently, the value of k1 was estimated from a competition experiment in which the effect of GW0385 on the binding of E to saquinavir was determined The value of k1 for GW0385 was estimated from these expts. to be 137±4 μM-1 s-1. Because E·[3H]GW0385 was stable in the standard buffer at room temperature for greater than 33 days, the value of the first-order rate constant for dissociation of E·[3H]GW0385 (k-1) could be estimated from the time-course for exchange of E·[3H]GW0385 with excess unlabeled GW0385. The value of k-1 calculated from these data was (2.1±0.1) + 10-6 s-1 (t1/2 = 91 h). The Ki value of wild-type HIV-1 protease for GW0385, calculated from these values for k1 and k-1, was 15±1 fM. Three multidrug resistant enzymes had Ki values for GW0385 that were less than 5 pM.
IT 810687-57-1P
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibition of wild-type and drug-resistant mutant human immunodeficiency virus type 1 proteases by GW0385 and other arylsulfonamides monitored by fluorescence)
RN 810687-57-1 HCAPLUS
CN Carbamic acid, [(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl-3-t]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

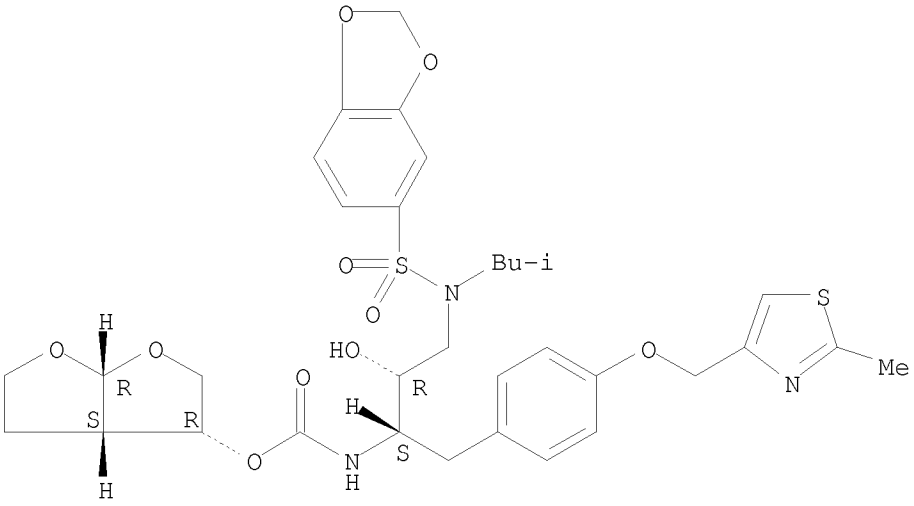


IT 313682-08-5, GW 0385
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(inhibition of wild-type and drug-resistant mutant human immunodeficiency virus type 1 proteases by GW0385 and other arylsulfonamides monitored by fluorescence)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

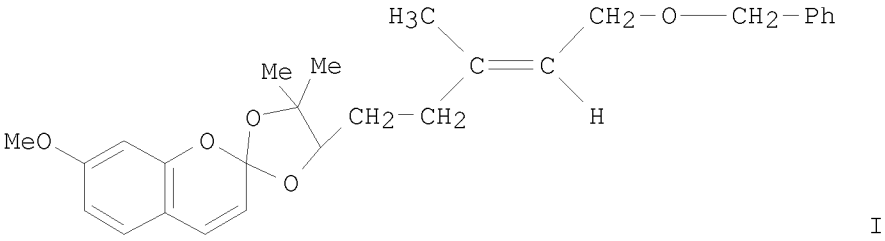
L14 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:252197 HCAPLUS
DOCUMENT NUMBER: 140:281350
TITLE: Spiro compounds for inhibiting the first-pass effect
INVENTOR(S): Harris, James W.
PATENT ASSIGNEE(S): Bioavailability System, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S. Ser. No. 793,416.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004058982	A1	20040325	US 2003-422848	20030425
US 6248776	B1	20010619	US 1999-251467	19990217
US 6476066	B1	20021105	US 2001-793416	20010227
US 2005214366	A1	20050929	US 2005-81024	20050316
US 7230027	B2	20070612		
US 2007244188	A1	20071018	US 2007-696198	20070404

PRIORITY APPLN. INFO.:

US 1999-251467	A3	19990217
US 2001-793416	A2	20010227
US 1997-56382P	P	19970826
US 1997-997259	A2	19971223
US 2003-422848	B1	20030425
US 2005-81024	A1	20050316

OTHER SOURCE(S): MARPAT 140:281350
GI



I

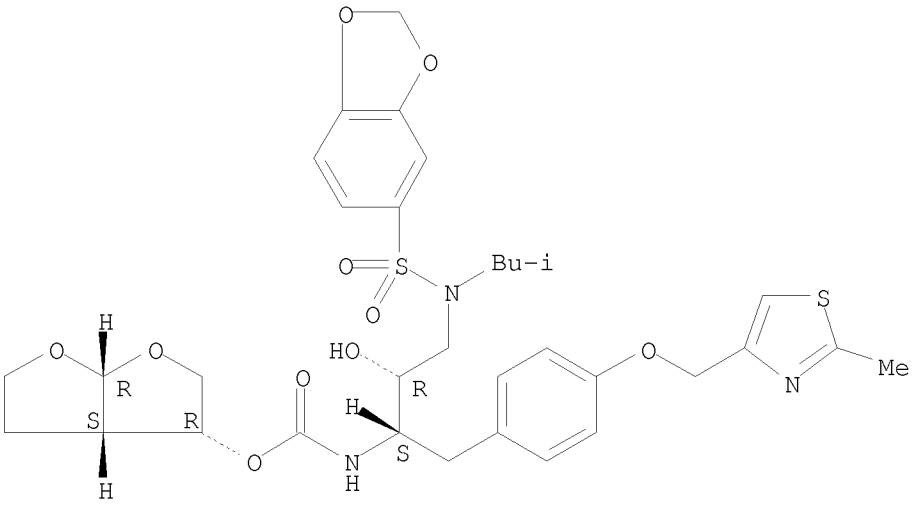
AB Compns., methods, etc. for addressing the first-pass effect are presented. An example compound prepared was I. Also processing citrus oils to obtain the compds. is given as examples as well as assessment of human cytochrome P 450-mediated biotransformation.

IT 313682-08-5, VX 385
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spiro compds. for inhibiting the first-pass effect)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:142902 HCAPLUS

DOCUMENT NUMBER: 140:187404

TITLE: Electrospun amorphous pharmaceutical compositions

INVENTOR(S): Ignatious, Francis; Sun, Linghong

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014304	A2	20040219	WO 2003-US24641	20030807
WO 2004014304	A3	20040624		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2494865	A1	20040219	CA 2003-2494865	20030807
AU 2003258120	A1	20040225	AU 2003-258120	20030807
EP 1534250	A2	20050601	EP 2003-784959	20030807
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013222	A	20050614	BR 2003-13222	20030807
CN 1684673	A	20051019	CN 2003-823237	20030807
JP 2005534716	T	20051117	JP 2004-527797	20030807
ZA 2005000563	A	20060726	ZA 2005-563	20050120
MX 2005PA01499	A	20050419	MX 2005-PA1499	20050207
US 2006013869	A1	20060119	US 2005-523835	20050207
US 2006083784	A1	20060420	US 2005-64890	20050224
NO 2005001123	A	20050506	NO 2005-1123	20050302
PRIORITY APPLN. INFO.:			US 2002-401726P P	20020807
			WO 2003-US24641 W	20030807
			US 2005-523835 A2	20050207

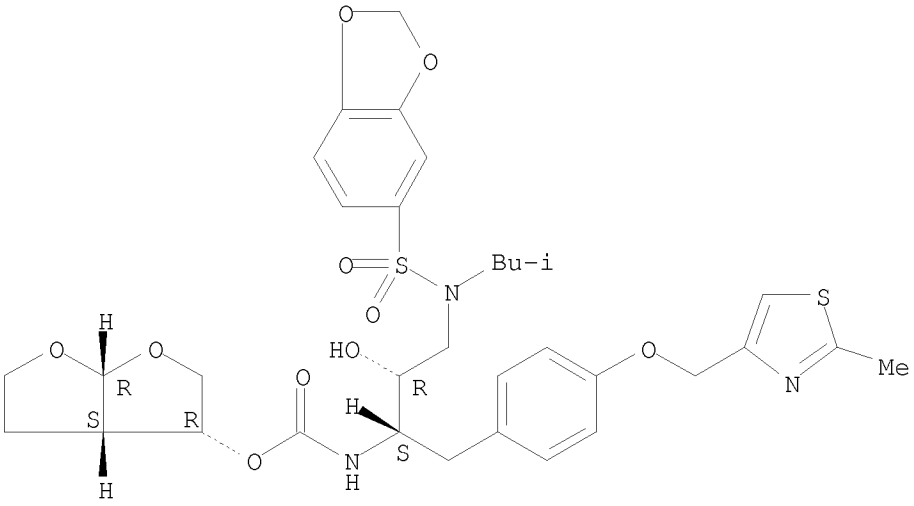
AB The present invention is directed to use of electrospinning, i.e. the process of making polymer nanofibers from either a solution or melt under elec. forces, to prepare stable, solid dispersions of amorphous drugs in polymer nanofibers. Thus, carvedilol-HBr monohydrate wa dissolved in THF and water. The solution was added to Polyox WSR1105 in MeCN solution This solution was spun to give nanofibers, and the morphol. of the drug was shown to be amorphous.

IT 313682-08-5
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(electrospun amorphous pharmaceutical compns.)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:900607 HCAPLUS
DOCUMENT NUMBER: 134:56676
TITLE: Preparation of arylsulfonamides as inhibitors of aspartyl protease
INVENTOR(S): Hale, Michael Robin; Tung, Roger; Price, Stephen; Wilkes, Robin David; Schairer, Wayne Carl; Jarvis, Ashley Nicholas; Spaltenstein, Andrew; Furfine, Eric Steven; Samano, Vicente; Kaldor, Istvan; Miller, John Franklin; Brieger, Michael Stephen
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Inc., USA; et al.
SOURCE: PCT Int. Appl., 396 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076961	A1	20001221	WO 2000-US15781	20000608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2380858	A1	20001221	CA 2000-2380858	20000608
BR 2000011745	A	20020319	BR 2000-11745	20000608
EP 1194404	A1	20020410	EP 2000-941279	20000608
EP 1194404	B1	20060503		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

	IE, SI, LT, LV, FI, RO, CY				
TR	200200407	T2	20020821	TR 2002-407	20000608
JP	2003502309	T	20030121	JP 2001-503821	20000608
TR	200202528	T2	20030221	TR 2002-2528	20000608
HU	2003000385	A2	20030728	HU 2003-385	20000608
HU	2003000385	A3	20070529		
NZ	516003	A	20040227	NZ 2000-516003	20000608
TW	593248	B	20040621	TW 2000-89111145	20000608
AU	779994	B2	20050224	AU 2000-56006	20000608
IN	2000CA00336	A	20050311	IN 2000-CA336	20000608
AT	325091	T	20060615	AT 2000-941279	20000608
EP	1686113	A1	20060802	EP 2006-9072	20000608
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PT	1194404	T	20060831	PT 2000-941279	20000608
ES	2263478	T3	20061216	ES 2000-941279	20000608
TR	200603871	T2	20070122	TR 2006-3871	20000608
US	6878728	B1	20050412	US 2000-591464	20000609
IN	2001KN01289	A	20050311	IN 2001-KN1289	20011206
NO	2001006034	A	20020118	NO 2001-6034	20011210
NO	323951	B1	20070723		
MX	2001PA12808	A	20020722	MX 2001-PA12808	20011211
ZA	2001010177	A	20030113	ZA 2001-10177	20011211
KR	762188	B1	20071004	KR 2001-716293	20011211
HK	1046899	A1	20070302	HK 2002-106939	20020923
US	2004122000	A1	20040624	US 2003-691333	20031021
IN	2007KN00501	A	20070706	IN 2007-KN501	20070209

PRIORITY APPLN. INFO.:	US 1999-139070P	P	19990611
	US 2000-190211P	P	20000317
	EP 2000-941279	A3	20000608
	WO 2000-US15781	W	20000608
	US 2000-591464	A3	20000609
	IN 2001-KN1289	A3	20011206

OTHER SOURCE(S): MARPAT 134:56676

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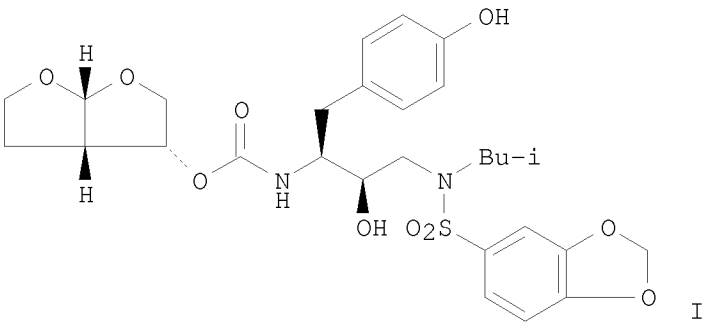


I

AB The title arylsulfonamides, namely (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 3-arylsulfonylamino-1-(4-hydroxyphenyl)-2-hydroxypropylcarbamate derivs. (e.g. I) are prepared These compds. are particularly well suited for inhibiting HIV-1 and HIV-2 protease activity and consequently, may be advantageously used as anti-viral agents against the HIV-1 and HIV-2 viruses. They are useful for treating with a patient diagnosed with AIDS,

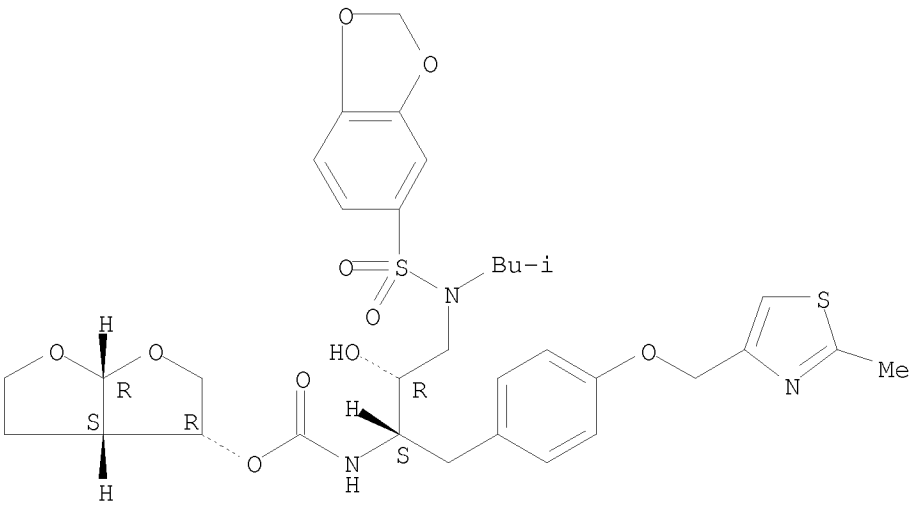
AIDS related complex (ARC), progressive generalized lymphadenopathy (PGL), Kaposi's sarcoma, thrombocytopenic purpura, or AIDS-related neurol. conditions such as AIDS dementia complex, multiple sclerosis or tropical paraperesis, etc. Thus, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 3-[N-(1,3-benzodioxol-5-ylsulfonyl)-N-isobutylamino]-1-(4-hydroxyphenyl)-2-hydroxypropylcarbamate underwent Mitsunobu reaction with phenethyl alc. using Ph3P and di-tert-Bu azodicarbonate in CH2Cl2 at room temperature for 1.5 h to give 72% I. I showed IC50 of <0.001, <0.001, and 0.01-0.001 μM against drug-resistant HIV strains, i.e. wild type, mutant HIV-1 EP13, and mutant D545701-14 HIV strains, resp., in MT-4 cells.

IT 313682-08-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylsulfonamides as inhibitors of HIV aspartyl protease and antiviral agents)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	332.31	573.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-47.20	-47.20

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STN INTERNATIONAL SESSION SUSPENDED AT 16:01:15 ON 05 FEB 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJRK1626

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'HCAPLUS' AT 16:13:32 ON 05 FEB 2008
FILE 'HCAPLUS' ENTERED AT 16:13:32 ON 05 FEB 2008
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	332.31	573.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-47.20	-47.20

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	332.31	573.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-47.20	-47.20

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DICTIONARY FILE UPDATES: 4 FEB 2008 HIGHEST RN 1001463-85-9

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experimental property data in the original document. For information

on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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chain nodes :
9 10
ring nodes :
1 2 3 4 5 6 7 8
chain bonds :
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ring bonds :
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exact/norm bonds :
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exact bonds :
9-10

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS

L16 STRUCTURE UPLOADED

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FULL SCREEN SEARCH COMPLETED - 15 TO ITERATE

100.0% PROCESSED 15 ITERATIONS 7 ANSWERS
SEARCH TIME: 00.00.01

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=> file hcaplus

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CA SUBSCRIBER PRICE	0.00	-47.20

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FILE COVERS 1907 - 5 Feb 2008 VOL 148 ISS 6
FILE LAST UPDATED: 4 Feb 2008 (20080204/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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L3   STRUCTURE UPLOADED
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L6   2 L1 EXA FULL
L7   8 L2 EXA FULL
L8   1 L3 EXA FULL
L9   1 L4 EXA FUL

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L18 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1275513 HCAPLUS
DOCUMENT NUMBER: 147:502340
TITLE: Process for preparation of carbamic acid bisfuranyl esters as HIV protease inhibitors and their use in the treatment of retroviral infection
INVENTOR(S): Crawford, Kenneth R.; Dowdy, Eric D.; Gutierrez, Arnold; Polniaszek, Richard P.; Yu, Richard Hung Chiu
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007126812	A2	20071108	WO 2007-US7564	20070329
WO 2007126812	A3	20071221		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 2008004242	A1	20080103	US 2007-729522	20070329

PRIORITY APPLN. INFO.: US 2006-787126P P 20060329
OTHER SOURCE(S): CASREACT 147:502340
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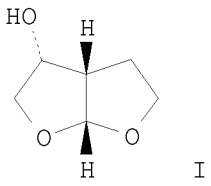

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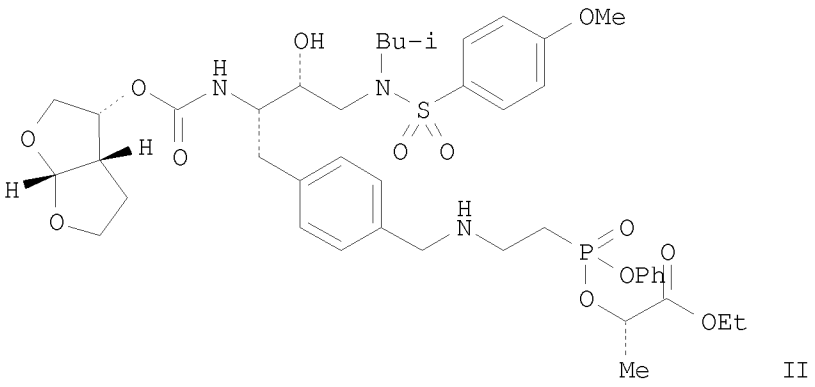


II

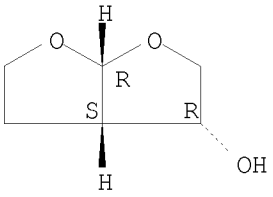
AB A process for the synthesis of bisfuran intermediates, e.g., I useful for preparing antiviral HIV protease inhibitor compds. is hereby disclosed. Example compound II was prepared as adipic acid salt and succinic acid salts, using intermediate I as the key component in the preparation The invention compds. were evaluated for their HIV protease inhibitory activity (no data).

IT 156928-09-5P
RL: BSU (Biological study, unclassified); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbamic acid bisfuranyl ester compds. as HIV protease inhibitors useful in treatment and prevention of retroviral infection)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

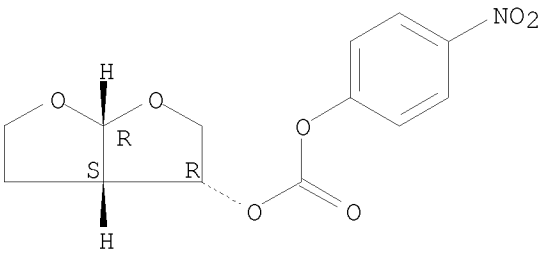
Absolute stereochemistry. Rotation (-).



IT 192725-55-6P
RL: BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbamic acid bisfuranyl ester compds. as HIV protease

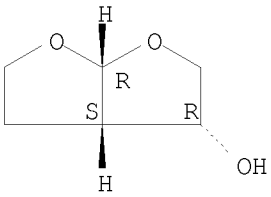
inhibitors useful in treatment and prevention of retroviral infection)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



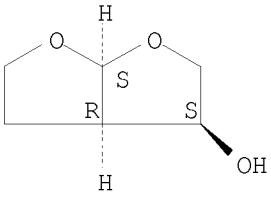
L18 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1131417 HCAPLUS
DOCUMENT NUMBER: 148:33642
TITLE: Research and Development of an Efficient Synthesis of Hexahydrofuro[2,3-b]furan-3-ol Moiety-A Key Component of the HIV Protease Inhibitor Candidates
AUTHOR(S): Yu, Richard H.; Polniaszek, Richard P.; Becker, Mark W.; Cook, Charles M.; Yu, Lok Him L.
CORPORATE SOURCE: Process Research Department, Gilead Sciences, Inc., Foster City, CA, 94404, USA
SOURCE: Organic Process Research & Development (2007), 11(6), 972-980
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 148:33642
AB A highly efficient method for the synthesis of racemic hexahydrofuro[2,3-b]furan-3-ol has been developed utilizing a lanthanide catalyst, such as Yb(fod)3, to promote condensation of 2,3-dihydrofuran and glycolaldehyde dimer. Access to either optically enriched enantiomer of bisfuran alc. can be obtained by using this method employing chiral ligands with the lanthanide catalyst. This method has been demonstrated to be a robust and scalable process with potential application for the construction of a variety of furo[2,3-b]furan derivs.
IT 156928-09-5P
RL: BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)
RN 156928-09-5 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



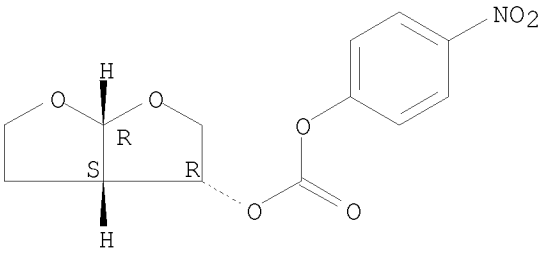
IT 162119-33-7P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)
RN 162119-33-7 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



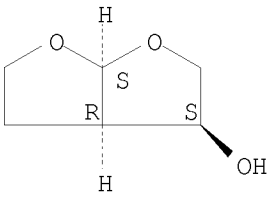
IT 192725-55-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 156928-10-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)
RN 156928-10-8 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

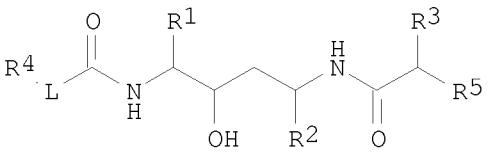


REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:449362 HCAPLUS
DOCUMENT NUMBER: 145:8179
TITLE: Process for the preparation of pyrimidinyl aminodiphenylhexane derivatives as retroviral protease inhibiting prodrugs
INVENTOR(S): Kumar, Gondi N.; Herrin, Thomas R.; Kempf, Dale J.; Betebenner, David A.; Chen, Xiaoqi; Norbeck, Daniel W.; Sham, Hing Leung; Patel, Ketan M.; Liu, Jih-Hua; Tien, Jieh-Heh J.; Stoner, Eric J.; Stengel, Peter J.; Plata, Daniel J.; Oliver, Patricia A.; Kolaczkowski, Lawrence; Hannick, Steven M.; Dickman, Daniel A.; Cooper, Arthur J.; Condon, Stephen L.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: Aust. Pat. Appl., 252 pp.
CODEN: AUXXCM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 2004201149	A1	20040422	AU 2004-201149	20040318
AU 2004201149	B2	20070802		
AU 2007231810	A1	20071129	AU 2007-231810	20071101
PRIORITY APPLN. INFO.:			AU 2001-13690 A3	20010112
			AU 2004-201149 A3	20040318
OTHER SOURCE(S):	MARPAT 145:8179			

GI



I

AB Pyrimidinyl aminodiphenylhexane derivs. I, wherein R1 and R2 are independently lower alkyl, cycloalkyl-alkyl, aryl-alkyl; R3 is lower

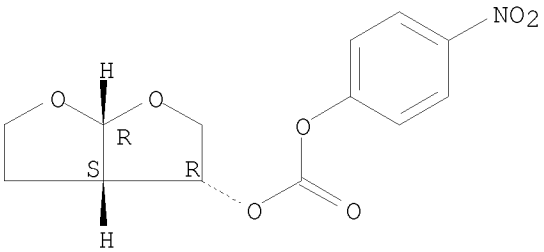
alkyl, cycloalkyl-alkyl, hydroxy-alkyl; R4 is aryl, heterocyclic; R5 is five- or six-membered heterocycle containing at least one nitrogen atom; L is O, S, NH, N-alkyl, , N-cycloalkyl, N-cycloalkyl-alkyl, O-alkylenyl, SO-alkylenyl, S(O)2-alkylenyl, alkylenyl-O, alkylenyl-S, alkylenyl, alkenylenyl, were prepared and tested in vitro and in human as retroviral protease inhibiting prodrugs. Thus, (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-[2S-(1-tetrahydropyrimid-2-onyl)-3-methylbutanoyl]amino-1,6-diphenylhexane was prepared via coupling of (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-amino-1,6-diphenylhexane with 2S-(1-tetrahydro-pyrimid-2-onyl)-3-methylbutanoic acid. The present invention relates to novel compds. and a composition and method for inhibiting retroviral proteases and in particular for inhibiting human immunodeficiency virus (HIV) protease, a composition and method for inhibiting a retroviral infection and in particular an HIV infection, processes for making the compds. and synthetic intermediates employed in the processes. While the compound of the invention can be administered as the sole active pharmaceutical agent, it can also be used in combination with one or more immunomodulators, antiviral agents, other antiinfective agents, or vaccines. The compds. of the invention are useful for inhibiting retroviral protease, in particular HIV protease, in vitro or in vivo (especially in mammals and in particular in humans). Total daily dose administered to a human or other mammal host in single or divided doses may be in amts., for example, from 0.001 to 300 mg/kg body weight daily and more usually 0.1 to 20 mg/kg body weight daily.

IT 192725-55-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of pyrimidinyl aminodiphenylhexane derivs. as retroviral protease inhibiting prodrugs)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

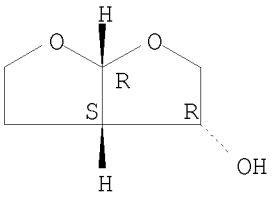


IT 156928-09-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of pyrimidinyl aminodiphenylhexane derivs. as retroviral protease inhibiting prodrugs)

RN 156928-09-5 HCAPLUS

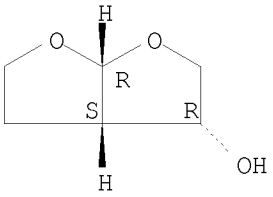
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L18 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:589326 HCAPLUS
DOCUMENT NUMBER: 143:267225
TITLE: Novel P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles
AUTHOR(S): Miller, John F.; Brieger, Michael; Furfine, Eric S.; Hazen, Richard J.; Kaldor, Istvan; Reynolds, David; Sherrill, Ronald G.; Spaltenstein, Andrew
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(15), 3496-3500
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:267225
AB A novel series of tyrosine-derived HIV protease inhibitors was synthesized and evaluated for in vitro antiviral activity against wild-type virus and two protease inhibitor-resistant viruses. All of the compds. had wild-type antiviral activities that were similar to or greater than several currently marketed HIV protease inhibitors. In addition, a number of compds. in this series were more potent against the drug-resistant mutant viruses than they were against wild-type virus.
IT 156928-09-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles)
RN 156928-09-5 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

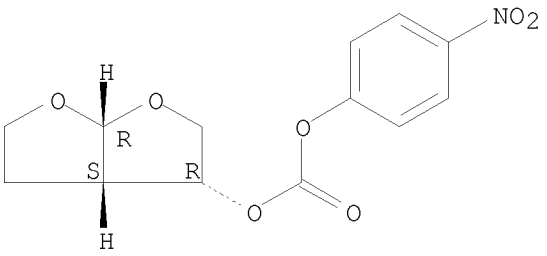
Absolute stereochemistry. Rotation (-).



IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:588404 HCAPLUS
DOCUMENT NUMBER: 143:133693
TITLE: Preparation of amino acid derivatives as HIV protease inhibitors
INVENTOR(S): Degoey, David A.; Flentge, Charles A.; Flosi, William J.; Grampovnik, David J.; Kempf, Dale J.; Klein, Larry L.; Yeung, Ming C.; Randolph, John T.; Wang, Xiu C.; Yu, Su
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 279 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

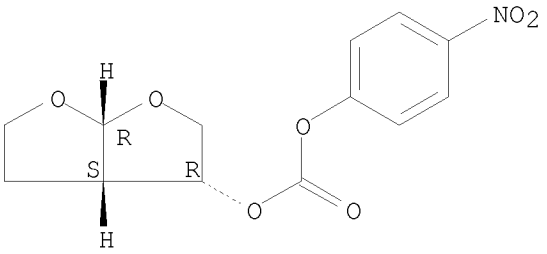
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005148623	A1	20050707	US 2004-8713		20041209
PRIORITY APPLN. INFO.:			US 2003-528974P	P	20031211

OTHER SOURCE(S): MARPAT 143:133693
AB The invention relates to amino acid derivs. A-NHCHR6CHR5CHR4CHR3NHCOCHR2NHCO2R1 [A is an amino acid or acyl residue of defined structure; R1, R2, R3, R6 are independently (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl or heteroaryl; R4, R5 are H (not both), OH or substituted hydroxyl], including pharmaceutically-acceptable salts, prodrugs or stereoisomers, having HIV protease inhibitory activity. Thus, Me (1S,4R,6S,7S,10S)-7-benzyl-1,10-di-tert-butyl-6-hydroxy-2,9,12-trioxo-4-[4-(2-pyridinyl)benzyl]-13-oxa-3,8,11-triazatetradec-1-ylcarbamate was prepared by a multistep procedure, which includes the reaction of intermediate tert-Bu (1S,2S,4R)-4-amino-1-benzyl-2-hydroxy-5-[4-(2-pyridinyl)phenyl]pentylcarbamate with N-protected L-tert-leucine. Compds. of the invention showed EC50 values in the range 0.7 nM to >3.2 μM

against wild-type HIV.

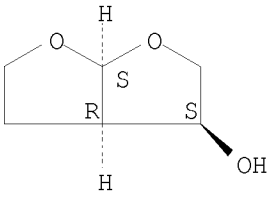
IT 192725-55-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as HIV protease inhibitors)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 162119-33-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid derivs. as HIV protease inhibitors)
RN 162119-33-7 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



L18 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:527398 HCAPLUS
DOCUMENT NUMBER: 143:78485
TITLE: Preparation of amino acid derivatives as HIV protease inhibitors
INVENTOR(S): Degoey, David A.; Flentge, Charles A.; Flosi, William J.; Grampovnik, David J.; Kempf, Dale J.; Klein, Larry L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 204 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005131017	A1	20050616	US 2003-733946	20031211
CA 2549098	A1	20050630	CA 2004-2549098	20041209
WO 2005058841	A2	20050630	WO 2004-US41658	20041209
WO 2005058841	A3	20060309		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1697344	A2	20060906	EP 2004-813910	20041209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
JP 2007516260	T	20070621	JP 2006-544070	20041209
MX 2006PA06612	A	20060831	MX 2006-PA6612	20060609

PRIORITY APPLN. INFO.: US 2003-733946 A 20031211
WO 2004-US41658 W 20041209

OTHER SOURCE(S): CASREACT 143:78485; MARPAT 143:78485

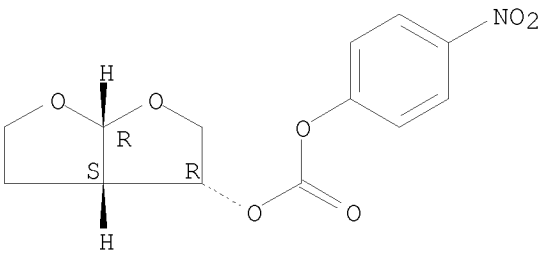
AB The invention relates to amino acid derivs. A-NHCHR6CHR5CHR4CHR3NHCOCHR2NHCO2R1 [A is an amino acid or acyl residue of defined structure; R1, R2, R3, R6 are independently (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl or heteroaryl; R4, R5 are H (not both), OH or substituted hydroxyl], including pharmaceutically-acceptable salts, stereoisomers, esters or prodrugs, having HIV protease inhibitory activity. Thus, Me (1S,4R,6S,7S,10S)-7-benzyl-1,10-di-tert-butyl-6-hydroxy-2,9,12-trioxo-4-[4-(2-pyridinyl)benzyl]-13-oxa-3,8,11-triazatetradec-1-ylcarbamate was prepared by a multistep procedure, which includes the reaction of intermediate tert-Bu (1S,2S,4R)-4-amino-1-benzyl-2-hydroxy-5-[4-(2-pyridinyl)phenyl]pentylcarbamate with N-protected L-tert-leucine. Compds. of the invention showed EC50 values 0.7-300 nM against wild-type HIV.

IT 192725-55-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as HIV protease inhibitors)

RN 192725-55-6 HCAPLUS

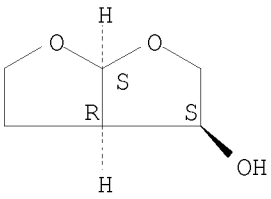
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 162119-33-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid derivs. as HIV protease inhibitors)
RN 162119-33-7 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



L18 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:14172 HCAPLUS
DOCUMENT NUMBER: 142:114047
TITLE: A preparation of furofuranyl derivative, useful as inhibitor of HIV aspartyl protease
INVENTOR(S): Roberts, John Charles; Toczko, Jennifer Fell
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; Martin, Michael Tolar
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000249	A2	20050106	WO 2004-US20353	20040625
WO 2005000249	A3	20050407		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
EP 1638960 A2 20060329 EP 2004-777060 20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR
JP 2007521277 T 20070802 JP 2006-517643 20040625
US 2006148865 A1 20060706 US 2005-560500 20051212
PRIORITY APPLN. INFO.: US 2003-483002P P 20030627
WO 2004-US20353 W 20040625
OTHER SOURCE(S): CASREACT 142:114047
GI

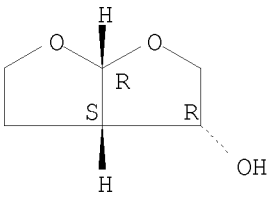
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of furofuranyl derivative I, useful as inhibitor of HIV aspartyl protease (no biol. data). For instance, I was prepared via deprotection of II and coupling with III with a yield of 90% (example 2).

IT 156928-09-5P 192725-55-6P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)

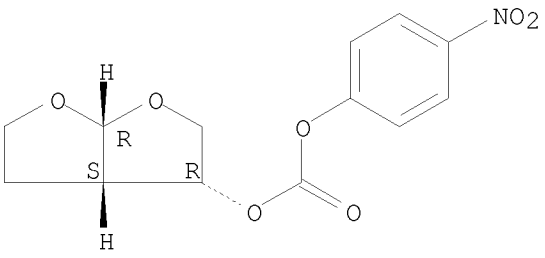
RN 156928-09-5 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

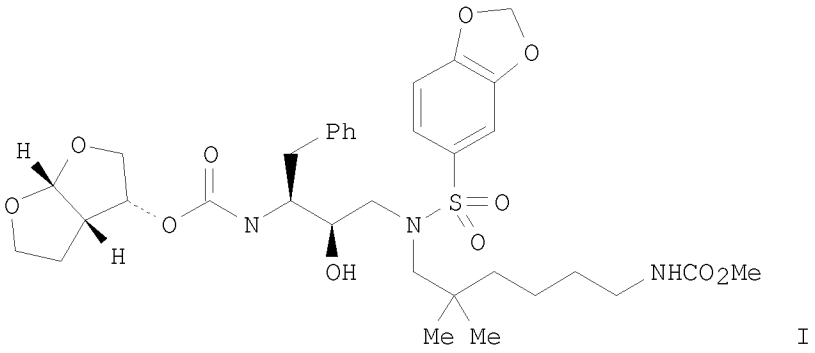


RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



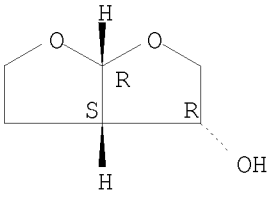
L18 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:99287 HCAPLUS
DOCUMENT NUMBER: 140:339141
TITLE: Novel arylsulfonamides possessing sub-picomolar HIV protease activities and potent anti-HIV activity against wild-type and drug-resistant viral strains
AUTHOR(S): Miller, John F.; Furfine, Eric S.; Hanlon, Mary H.; Hazen, Richard J.; Ray, John A.; Robinson, Laurence; Samano, Vicente; Spaltenstein, Andrew
CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(4), 959-963
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:339141
GI



I

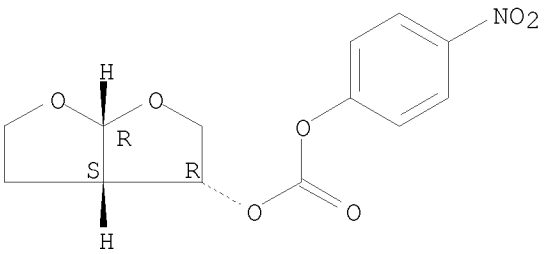
AB Furanofuryl analogs of the HIV protease inhibitor amprenavir such as I are prepared in which a terminally substituted n-alkyl group is appended to the N-iso-Bu group of amprenavir and in which the substituents on the N-arylsulfonyl moiety are varied. Some of the inhibitors such as I are found to have greatly enhanced inhibition of HIV protease; the amprenavir analogs also inhibit the growth of both wild-type and resistant strains of HIV and are more effective against the HIV strains than the currently marketed HIV protease inhibitors amprenavir, indinavir, and nelfinavir. E.g., I inhibits wild-type HIV protease with a Ki value of 0.014 pM, and inhibits wild-type and resistant strains of HIV with IC50 values of between 1.6 nM and 15 nM.
IT 156928-09-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of furanofuryl amprenavir analogs with modifications at the N-arylsulfonyl and N-iso-Bu moieties which show improved HIV protease inhibition and inhibition of wild-type and resistant HIV strains)
RN 156928-09-5 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of furanofuryl amprenavir analogs with modifications at the N-arylsulfonyl and N-iso-Bu moieties which show improved HIV protease inhibition and inhibition of wild-type and resistant HIV strains)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:811207 HCAPLUS
DOCUMENT NUMBER: 132:49801
TITLE: Preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compounds as inhibitors of HIV aspartyl protease.
INVENTOR(S): Sherrill, Ronald George; Hale, Michael R.; Spaltenstein, Andrew; Furfine, Eric Steven; Andrews, Clarence Webster, III; Lowen, Gregory Thomas
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 344 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965870	A2	19991223	WO 1999-US13744	19990617

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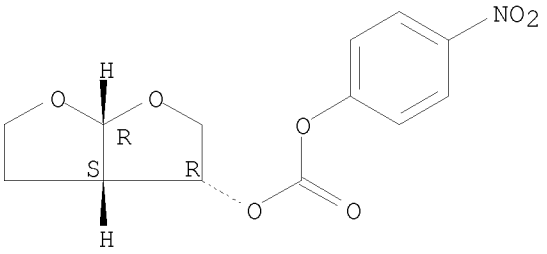
     WO 9965870           A3    20010315
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
             JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2335477           A1    19991223    CA 1999-2335477        19990617
     AU 9945760           A     20000105    AU 1999-45760          19990617
     AU 767728            B2    20031120
     EP 1086076           A1    20010328    EP 1999-928769         19990617
     EP 1086076           B1    20041222
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     BR 9912169           A     20010410    BR 1999-12169          19990617
     NZ 508855            A     20031031    NZ 1999-508855         19990617
     AT 285396            T     20050115    AT 1999-928769         19990617
     PT 1086076           T     20050531    PT 1999-928769         19990617
     ES 2235492           T3    20050701    ES 1999-928769         19990617
     AP 1717              A     20070228    AP 2000-2023           19990617
     US 2002049201        A1    20020425    US 2000-731129         20001206
     US 6613743           B2    20030902
     NO 2000006405        A     20010219    NO 2000-6405           20001215
     MX 2000PA12637       A     20010405    MX 2000-PA12637        20001218
     HK 1037605           A1    20051007    HK 2001-106764         20010925
     US 2004097594        A1    20040520    US 2003-600937         20030620
     NZ 528074            A     20041126    NZ 2003-528074         20030908
     AU 2004200636        A1    20040311    AU 2004-200636         20040219
     US 2006172936        A1    20060803    US 2005-212045         20050825
     AU 2007234578        A1    20071213    AU 2007-234578         20071121
PRIORITY APPLN. INFO.:                      US 1998-90094P      P  19980619
                                            WO 1999-US13744     W  19990617
                                            US 2000-731129      A3 20001206
                                            US 2003-600937      B3 20030620
                                            AU 2004-200636      A3 20040219

OTHER SOURCE(S):         MARPAT 132:49801
AB   ABxN(Gx)CHDCHOR7CH2ND'SO2E [A = H, (substituted) Ht, R1Ht, R1Ak; Ak =
     alkyl; Ht = cycloalkyl, cycloalkenyl, (substituted) aryl, heterocyclyl; R1
     = CO, SO2, COCO, O2C, NR2CO, NR2SO2, etc.; B = null, NR2C(R3)2CO; x = 0,
     1; R2 = H, (substituted) Ht, alkyl; R3 = H, (substituted) Ht, alkyl,
     alkenyl, cycloalkyl, cycloalkenyl; G = null, H, R7, alkyl; G may be bound
     to R7; D = (substituted) Q, alkyl, alkenyl; Q = (substituted) carbocyclyl,
     heterocyclyl; D' = OR10, N:R10, N(R10)R1R3; E = Ht, OHt, OR3, NR2R3,
     (substituted) alkyl, alkenyl, etc.; R7 = H, (CH2O)xY(ZM)(:X)Z(M)x, etc.; M
     = null, H, Li, Na, K, Mg, Ca, Ba, alkyl, alkenyl, etc.; X = O, S; Y = P,
     S; Z = O, S, N(R2)2, H], were prepared as inhibitors of HIV aspartyl
     protease (no data).  Thus, 3-H2NC6H4SO2NHOCHMe2 (preparation given), tert-Bu
     N-(1S)-1-[(2S)-oxiran-2-yl]-2-phenylethylcarbamate, and phosphazene base
     P4 tert-Bu were stirred in 8 h in THF to give 95% tert-Bu
     N-(1S,2R)-3-[[(3-aminophenyl)sulfonyl](isopropoxy)amino]-1-benzyl-2-
     hydroxypropylcarbamate.
IT   192725-55-6 252873-35-1 252873-40-8
     252873-50-0 252873-51-1
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-
```

hydroxypropanes and related compds. as inhibitors of HIV aspartyl protease)
RN 192725-55-6 HCAPLUS
CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 252873-35-1 HCAPLUS
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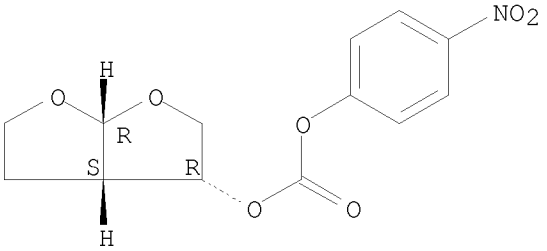
Relative stereochemistry.



RN 252873-40-8 HCAPLUS
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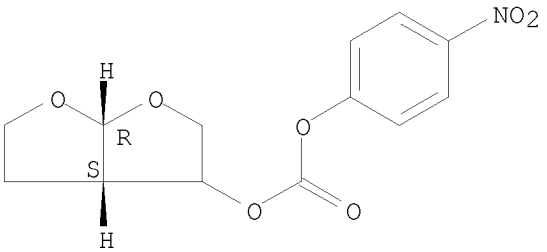
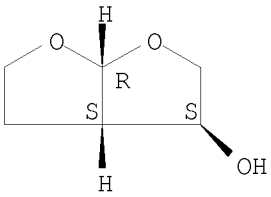
Absolute stereochemistry.



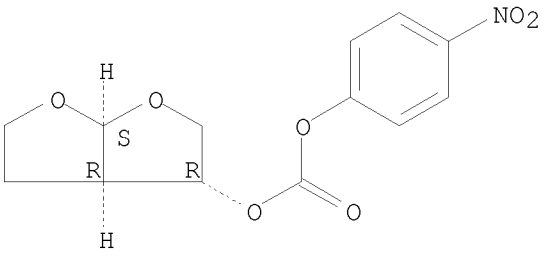
RN 252873-50-0 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



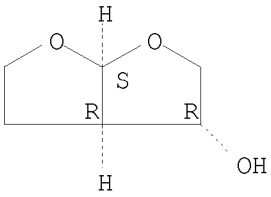
RN 252873-51-1 HCAPLUS
CN Carbonic acid, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



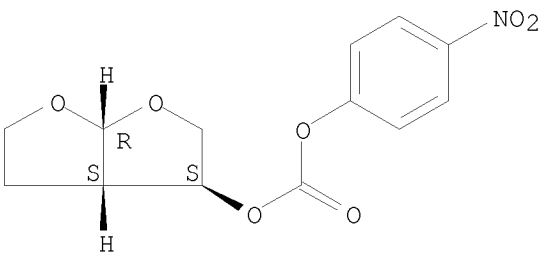
IT 252873-00-0P 252873-01-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compds. as inhibitors of HIV aspartyl protease)
RN 252873-00-0 HCAPLUS
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 252873-01-1 HCAPLUS
CN Carbonic acid, (3S,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:393986 HCAPLUS
DOCUMENT NUMBER: 131:59143
TITLE: Preparation of peptide analogs as retroviral protease inhibitors
INVENTOR(S): Sham, Hing Leung; Norbeck, Daniel W.; Chen, Xiaoqi; Betebenner, David A.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 572,226, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5914332	A	19990622	US 1996-753201	19961121
CA 2238978	A1	19970619	CA 1996-2238978	19961206
CA 2238978	C	20010515		
CA 2285119	A1	19970619	CA 1996-2285119	19961206
CA 2285119	C	20050920		
CA 2509505	A1	19970619	CA 1996-2509505	19961206
WO 9721685	A1	19970619	WO 1996-US20440	19961206
W: AU, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9713422	A	19970703	AU 1997-13422	19961206
AU 725369	B2	20001012		
EP 882024	A1	19981209	EP 1996-944941	19961206
EP 882024	B1	20020206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1208405	A	19990217	CN 1996-199904	19961206
HU 9901079	A2	19990928	HU 1999-1079	19961206
HU 223782	B1	20050128		
JP 2000502085	T	20000222	JP 1997-522278	19961206
JP 3170292	B2	20010528		
HU 20003305	A3	20001228	HU 2000-3305	19961206
HU 222731	B1	20030929		
JP 2001058979	A	20010306	JP 2000-190510	19961206
EP 1170289	A2	20020109	EP 2001-124290	19961206
EP 1170289	A3	20021113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AT 212986	T	20020215	AT 1996-944941	19961206

PT 882024	T	20020731	PT 1996-944941	19961206
ES 2173341	T3	20021016	ES 1996-944941	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
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NZ 510329	A	20040227	NZ 1996-510329	19961206
CZ 293650	B6	20040616	CZ 2000-2210	19961206
CZ 294246	B6	20041110	CZ 1998-1762	19961206
NZ 510328	A	20050128	NZ 1996-510328	19961206
IL 156237	A	20050517	IL 1996-156237	19961206
NZ 338003	A	20050826	NZ 1996-338003	19961206
CZ 296915	B6	20060712	CZ 2004-762	19961206
ZA 9610475	A	19970731	ZA 1996-10475	19961212
TW 494097	B	20020711	TW 1997-86101654	19970213
TW 259178	B	20060801	TW 2000-89115157	19970213
US 6284767	B1	20010904	US 1998-207873	19981208
HK 1016585	A1	20020809	HK 1999-101462	19990409
US 6313296	B1	20011106	US 2000-511390	20000223
US 2002004503	A1	20020110	US 2001-837280	20010418
US 6472529	B2	20021029		
US 2003100755	A1	20030529	US 2002-280652	20021025
US 7279582	B2	20071009		

PRIORITY APPLN. INFO.:	US 1995-572226	B2	19951213
	US 1996-753201	A	19961121
	US 1996-754687	A	19961121
	CA 1996-2238978	A3	19961206
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	EP 1996-943605	A3	19961206
	EP 1996-944941	A3	19961206
	IL 1996-124607	A3	19961206
	JP 1997-522278	A3	19961206
	WO 1996-US20440	W	19961206
	US 1998-207873	A3	19981208
	US 2001-837280	A3	20010418

OTHER SOURCE(S): MARPAT 131:59143

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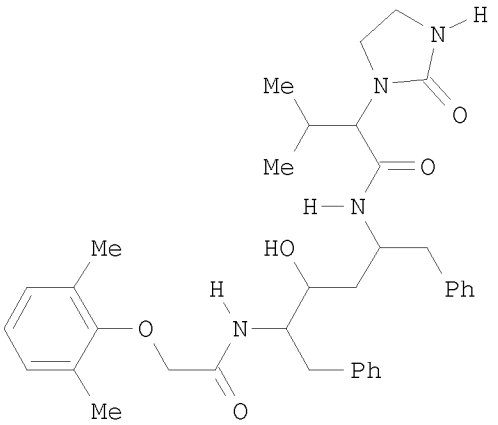


II

AB R4Z1CONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [I; R1,R2 = lower alkyl,

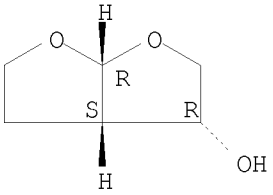
cycloalkylalkyl, arylalkyl; R3 = lower alkyl, hydroxyalkyl, cycloalkylalkyl; R4 = aryl, heterocyclyl; R5 = N-attached (thi)oxo- or iminoazacycloalkyl; Z1 = Z, O, S, (alkyl)imino, OZ, ZO, NHZ, etc.; Z = alkylene] were prepared Thus, title compound (S,S,S)-II was prepared in 8 steps from L-phenylalanine. Data for biol. activity of I were given.

IT 156928-09-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

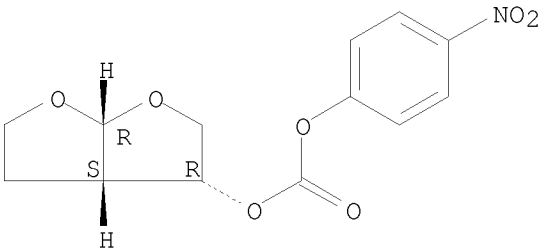


IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:515728 HCAPLUS

DOCUMENT NUMBER: 127:122001

TITLE: Preparation of peptide analogs as retroviral protease inhibitors

INVENTOR(S): Sham, Hing Leung; Norbeck, Daniel W.; Chen, Xiaoqi; Betebenner, David A.; Kempf, Dale J.; Herrin, Thomas R.; Kumar, Gondi N.; Condon, Stephen L.; Cooper,

Arthur J.; Dickman, Daniel A.; Hannick, Steven M.; Kolaczkowski, Lawrence; Oliver, Patricia A.; Plata, Daniel J.; Stengel, Peter J.; Stoner, Eric J.; Tien, Jieh-Heh J.; Liu, Jih-Hua; Patel, Ketan M.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721685	A1	19970619	WO 1996-US20440	19961206
W: AU, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5914332	A	19990622	US 1996-753201	19961121
AU 9713422	A	19970703	AU 1997-13422	19961206
AU 725369	B2	20001012		
EP 882024	A1	19981209	EP 1996-944941	19961206
EP 882024	B1	20020206		
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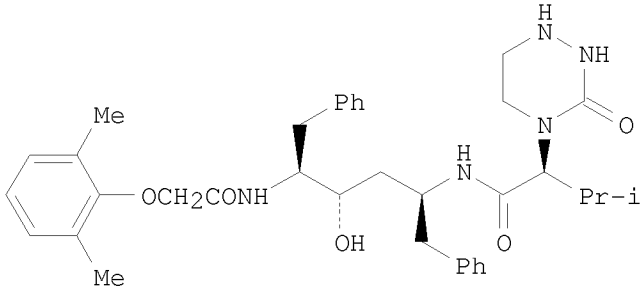
HU 9901079	A2	19990928	HU 1999-1079	19961206
HU 223782	B1	20050128		
JP 2000502085	T	20000222	JP 1997-522278	19961206
JP 3170292	B2	20010528		
HU 20003305	A3	20001228	HU 2000-3305	19961206
HU 222731	B1	20030929		
AT 212986	T	20020215	AT 1996-944941	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
IL 156237	A	20050517	IL 1996-156237	19961206
HK 1016585	A1	20020809	HK 1999-101462	19990409

PRIORITY APPLN. INFO.:	US 1995-572226	A	19951213
	US 1996-753201	A	19961121
	US 1996-754687	A	19961121
	EP 1996-943605	A3	19961206
	IL 1996-124607	A3	19961206
	WO 1996-US20440	W	19961206

OTHER SOURCE(S): MARPAT 127:122001
GI



I

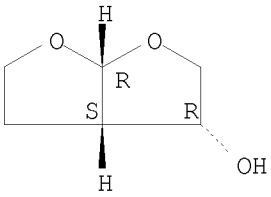
AB R4 -L1-CONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [R1, R2 = lower alkyl, cycloalkylalkyl, arylalkyl; R3 = lower alkyl, hydroxyalkyl, cycloalkylalkyl; R4 = aryl, heterocyclyl; R5 = heterocyclyl e.g. Q - Q4; wherein m, n = 1-3; p = 1,2; X = O, S, NH; Y = CH2, O, S, (un)substituted NH; Z = O, S, NH; L1 = O, S, (un)substituted NH, O-alkylenyl, S(O)m-alkylenyl (wherein m = 0, 1,2), N-(un)substituted NH-alkylenyl, alkylenyl, alkenylenyl, etc.] are prepared Methods and compns. for inhibiting an HIV infection are also disclosed. Thus, (2S)-(4-benzyloxycarbonylaza-1-tetrahydropyrimid-2-onyl)-3-methylbutanoic acid (preparation given) was condensed with (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-amino-1,6-diphenylhexane using standard coupling procedure [1-ethyl-3-(3-dimethylaminopropyl)carbodiimide/DMF] followed by hydrogenolysis over 10% Pd-C to give the title compound (I). I in vitro at 0.5 nmol inhibited HIV protease by 94.6%.

IT 156928-09-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

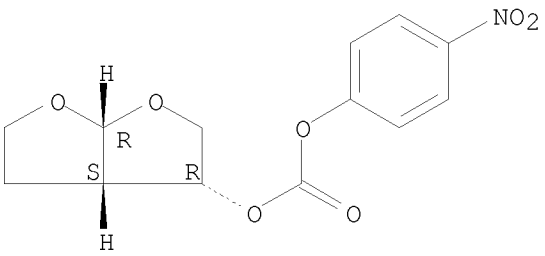


IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L18 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN

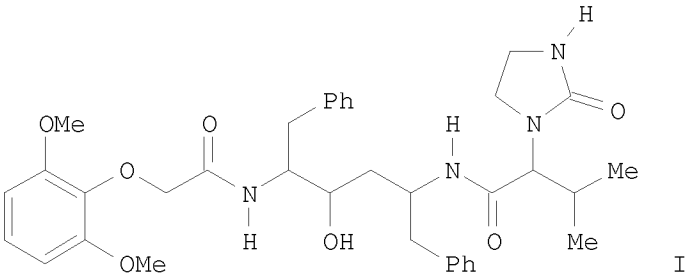
ACCESSION NUMBER: 1997:515727 HCAPLUS
DOCUMENT NUMBER: 127:121994
TITLE: Preparation and formulation of N-(α-aminoacyl)diaminohydroxyalkanes as HIV protease inhibitors
INVENTOR(S): Sham, Hing Leung; Stewart, Kent D.; Kempf, Dale J.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721683	A1	19970619	WO 1996-US19394	19961206
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2238977	A1	19970619	CA 1996-2238977	19961206
EP 876353	A1	19981111	EP 1996-943605	19961206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000502997	T	20000314	JP 1997-522112	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.:

US 1995-572226	A	19951213
US 1996-754687	A	19961121
EP 1996-943605	A3	19961206
WO 1996-US19394	W	19961206

OTHER SOURCE(S): MARPAT 127:121994
GI



I

AB R4ZCONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [I; R1,R2 = (cyclo)alkyl, aralkyl; R3 = (cyclo)alkyl, hydroxyalkyl; R4 = heterocyclyl or aryl; R5 = N-attached oxoheterocyclyl, etc.] were prepared Thus, (S)-(PhCH2)2NCH(CH2Ph)COCH2CN (preparation given) was condensed with PhCH2MgCl and the product reduced by NaBH4 to give (S,S,S)-(PhCH2)2NCH(CH2Ph)CH(OH)CH2CH(NH2)CH2Ph. The latter was N-protected and the N-debenzylated product amidated by 2,6-(MeO)C6H3OCH2CO2H (preparation given) to give, after deprotection and amidation by (S)-Me2CHCHR5CO2H (R5 = 2-oxo-1H-imidazol-3-yl)(preparation

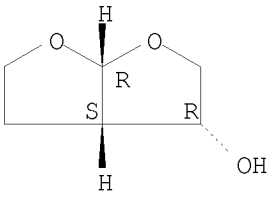
given), title compound (S,S,S,S)-II. Data for biol. activity of I were given.

IT 156928-09-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and formulation of N-(α-aminoacyl)diaminohydroxyalkanes as HIV protease inhibitors)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

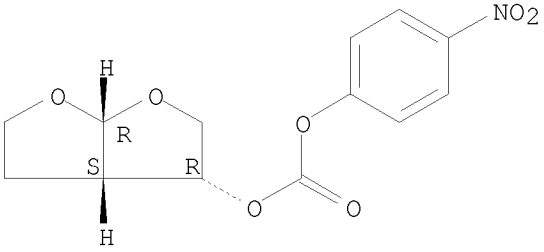


IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and formulation of N-(α-aminoacyl)diaminohydroxyalkanes as HIV protease inhibitors)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	68.09	702.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.60	-56.80

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 16:14:25 ON 05 FEB 2008